Axillary web syndrome after treatment for breast cancer: An exploration of imaging evidence of fascial changes and its relationship to clinical variables

by

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DECLARATION

I, Kyle Joseph Catharina Paulssen, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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QUOTATIONS

“Read in your anatomy the neglected story between the lines; that is the continuity.”
Dutch anatomist, Jaap van der Wal, on fascia

“… Therefore, following the destruction of the tissue, and the ensuing disorder, both the surgeon, by re-establishing correct anatomical relationships, and the manual therapist working with the tissues to restore flexibility, can bring about significant improvements, and restore meaning to the original fibrillar network.”
French surgeon, Dr Jean-Claude Guimberteau, on fascia

“The findings of fascia research show that the disregarded connective tissue includes the cause for inexplainable illnesses and pain, but also, an inexhaustible source of cure.”
Kirsten Esch, in the documentary “Fascinating Fasciae” by ARTE and ZDF, 2017

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KYLE PAULSSEN

ABSTRACT

Breast cancer is the most commonly diagnosed cancer in women and surgery remains the primary treatment. Evaluation of tumour spread is done by axillary lymph node assessment by surgical excision. Such invasive treatments, in conjunction with adjuvant therapies such as chemotherapy, radiotherapy and hormonal therapy, may alter patient healing patterns giving rise to complications such as axillary web syndrome (AWS).

AWS presents as a puckering web of axillary skin overlying a cord of tissue that tightens with shoulder abduction. It is painful, limits shoulder range of movement (ROM) and reduces the quality of life of the patients. The syndrome is elusive, does not occur in everyone and is thought to be self-limiting in nature with spontaneous cord resolution. Evidence, however, is pointing towards long-term morbidity in some patients. The cord itself has been hypothesised to be lymphatic or vascular in origin and damage during axillary surgery gives rise to the structure.

Anatomically, the vascular structures are bound by the connective tissue network of fascia. The adhesive and puckering appearance of the cord on clinical examination and in limited biopsy studies could imply a possible role of damaged fascia in the syndrome. The fascia, as a three-dimensional body-wide network, has been shown to be a functional unit with the musculoskeletal system and is important in coordinating movement. Furthermore, the fascia contains numerous receptors imperative for proprioceptive and nociceptive functioning. The fibroblast cells and fibres that it comprises are involved in tissue healing and scar tissue formation. Chronic inflammation upon fascial damage can lead to tissue adhesions and fibrosis, rendering a non-functional scar.

Ultrasonography (US) has been able to visualise fascial differences and has been used to examine fascial abnormalities including scars and adhesions. Physiotherapy treatment has been shown to aid in remobilising scar tissue and in being able to help improve morbidity in AWS patients. The authors therefore hypothesised that damaged fascia contributes to the symptomology of AWS. The present study set out to evaluate whether altered fascia plays a role in the syndrome using fascial explanations for risk factors in the AWS literature and US in patients with AWS to observe anatomical changes. Furthermore, the authors hypothesised that myofascial physiotherapy could aid in cord resolution and symptom improvement and that it would reflect in fascial changes on US.

The current descriptive, observational, pilot, proof-of-concept case-series study focused on fascial changes before and after myofascial release physiotherapy in women presenting with AWS

following breast cancer treatment (*n* = 11). At the time points, US in the area of interest (the axilla) and MRI scans of a single patient were done pre-physiotherapy. Furthermore, patient variables of ROM, pain and disability using the SPADI questionnaire, and quality of life using the FACT-B questionnaire, were evaluated to relate to any fascial differences between affected and unaffected arms on US and compared to findings after physiotherapy to determine trends. To observe fascial continuity, alignment of US scans was attempted.

The results from the case studies and overall trends indicated thickened fascia, reduced continuity, decreased gliding potential and increased adherence between the different fascial layers on US in the majority of patients on the affected arm in the area of interest suggesting that they are changes resulting from the treatment. The findings related to the external cord appearance. On MRI, a fibrous band of tissue was observed connecting to muscles and skin. The findings were found to descriptively show a trend with reduced ROM and increased SPADI scores. No descriptive relationship with FACT-B was noted.

Several patients (*n* = 6) continued with physiotherapy for six treatments. The treatment proved beneficial for all patients, who improved on ROM and SPADI scores. However, not all their symptoms were completely resolved. The findings corroborate observations on US showing improved gliding, more regular and organised fascia, and less adhesions post-physiotherapy. Cord resolution or reduction occurred in half of the patients.

Risk factors for AWS as identified in the literature and related to the patients, such as more invasive treatments and (neo)adjuvant therapies, were explained to cause more fibrosis and possibly contributed to the symptoms seen but could not be verified in the study due to the small, varied sample. Furthermore, due to the difficulty of finding suitable patients and the low sample size, the current study could not statistically corroborate many correlations and hence was limited to descriptive trend description.

Using the fascial literature, restricted fascia and adhesions could be explained to lead to biomechanical limitations, explaining reduced ROM and nociceptor activation as seen in pain reported in the study. A fibrosed vessel damaged during axillary surgery as well as surrounding fascial changes, which occurred as the result of the healing response, could explain the varying appearances of the cord.

The author concluded that the trends seen suggest a link for morbidity resulting from fascial damage and adds weight to the evidence of fascial involvement in AWS. Wider fascial involvement on US and MRI descriptively related to the presence of cording, limited shoulder ROM and pain before and improvements and changes in the domains after physiotherapy, supported the hypotheses. The present study highlighted that myofascial release can be beneficial for patients suffering from AWS and suggests that US may be a feasible outcome measure to aid in evaluating fascia and fibrosis subsequent to physiotherapy, guide it and determine its efficacy. Furthermore, risk factors need to be identified to implement an early warning system for the sequelae of breast cancer so that patients at risk are identified timeously and receive the help they need to minimise the effect of the syndrome on their wellbeing in order to improve their quality of life.

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Chapter 1: Introduction

1.1. Breast cancer and treatment

Female breast cancer is a worldwide problem with more than one million new diagnoses per year (Parkin *et al*., 1999). In South Africa it is the most commonly diagnosed cancer with 1 in 29 women at risk of developing the disease (Cancer Association of South Africa, 2004). The mainstay of breast cancer treatment remains surgery with the focus of invasively removing the local tumour and the assessment of axillary lymph node spread. The assessment is by sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) with the former being less destructive (Cheville & Tchou, 2007; Edge, 2004). Surgery may be used in conjunction with adjuvant or additional therapies such as radiotherapy and chemotherapy which may impact healing patterns (Cheville & Tchou, 2007). Despite that procedures have become more conservative, there are numerous complications that can arise from the treatments (Fourie & Robb, 2009). However, it is thought that clinicians often downplay the potentially debilitating effects the complications might have on a patient's life after they have already had to cope with cancer (Josenhans, 2007). As a result of the stance of the clinicians and the negligence of not assigning appropriate exercises, the patient may be wrongfully led to think that the symptoms they experience, such as limited range of movement (ROM) and pain, are normal. Normalisation often leads to worse complications and sometimes permanent morbidity (Kepics, 2007). The features mentioned are seen in a disorder called axillary web syndrome (AWS).

1.2. Axillary web syndrome (AWS)

Moskovitz and colleagues first described AWS in 2001 as "a visible web of axillary skin overlying [a] palpable [cord or] cords of tissue that are made taut by shoulder abduction" (Moskovitz *et al*., 2001 p. 435). They further describe the webbed cording as extending from the axilla down the ipsilateral arm sometimes as far as the thumb (Figure 1.1). The tissue is described as painful and tender to the touch, causing tightness and pulling on both the skin and contents of the axilla (Moskovitz *et al*., 2001). Other symptoms include axillary pain that radiates down the arm and greatly reduced ROM of the arm itself (Moskovitz *et al.*, 2001). Other authors describe AWS differently and include functional limitations and morbidity in their definitions (Lacomba *et al.*, 2009; Craythorne, Benton & Macfarlane, 2009). Practitioners in, especially, the manual therapies prefer to use the term "cording" as the cord is often found not to be limited to the axilla (Kepics, 2007) and can form in a completely different place such as over the arm or on the chest wall (Rashtak *et al.*, 2012). Most of the terms are often used interchangeably in the literature which leads to confusion as the term "cording" could only refer to the physical cord structure without accompanying symptoms. The uncertainty of the terminology also results in difficulties establishing prevalence in AWS.

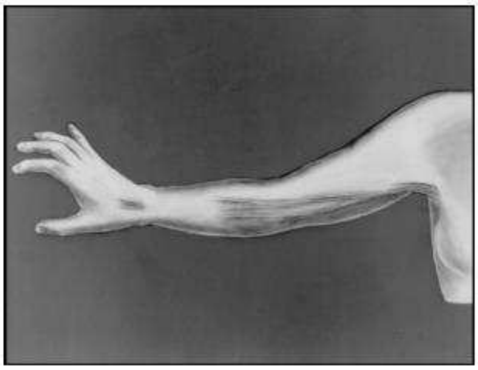


Figure 1.1. *Schematic of axillary web syndrome (AWS). Adapted from Moskovitz et al. (2001).*

1.2.1. Prevalence of AWS

A very wide range of prevalence of 6-72% has been reported for AWS following axillary dissection, ALND and SLNB, after breast cancer surgery (Severeid, 2007; Lacomba *et al.*, 2009; Bergmann *et al.*, 2012). Leidenius and colleagues (2003) report a 20% prevalence of AWS after SNLD and a 72% prevalence after complete clearance of the axilla, which Craythorne and colleagues (2009) corroborate. The discrepancy in the literature might come about because of the relatively small sample sizes (n < 100) of the studies, which may reduce their statistical power. Furthermore, the different contexts in which the studies have been done may relate to differences in surgical procedures. Alternatively, sometimes the cord(s) may not be visible or palpable on physical examination due to its/their extension into the trunk. It is also possible that the cord might go undetected due to an increased thickness of the adipose layer superficial to the cord in patients with raised BMI (> 25) or in patients with lymphoedema in whom the accumulated fluid might obstruct access and visibility to the cord (Leidenius *et al*., 2003; Koehler, 2013). Kepics (2007) describes that she observed patients who were thought to have lymphoedema but where the cord had actually deformed the skin giving it an oedematous appearance. An apparently higher prevalence of AWS is therefore plausible.

Although more destructive surgery – such as complete axillary clearance in which all the connective tissue, adipose tissue and lymph nodes are removed – seems to predispose the patient to AWS development (Koehler, 2013), other research points towards even minor surgery and inflammation as possible causative factors for the development of the syndrome (Rashtak *et al.*, 2012). Other variables that have shown a correlation with AWS include a low BMI (BMI < 25) and having had a radical mastectomy (Bergmann *et al*., 2012). AWS also seems to be associated with lymphoedema development (Bergmann *et al.*, 2012). Further exploration of the relationships between the risk factors and AWS is needed.

1.2.2. Aetiology of AWS

Moskovitz *et al*. (2001) hypothesised that the aetiology of AWS is the result of the disruption of superficial veins and/or lymphatics during axillary surgery. Histopathological findings in the literature showed the cord may represent thrombosis of a blood vessel (Shetty & Watson, 2001) or a fibrosed and stased lymph vessel (Josenhans, 2007). Marcus, Pawade and Vella (1990) described collagenous tissue on biopsy and most authors found fibrosis (Marcus, Pawade & Vella, 1990; Reedijk *et al*., 2006; Villamiel Capos *et al.*, 2008; Rashtak *et al.*, 2012). Kepics (2007) hypothesises that stasis in lymphatics can lead to lymphoedema and leaking of protein-rich fluid into the interstitium which would lead to fibrosis, the increased deposition of collagen on the vessel wall and formation of the hardened cord.

AWS is sometimes also suggested to be a variant of Mondor's disease because of its similar presentation with a cord, but with occurrence in a different location – predominantly the chest wall and legs (Conant *et al.*, 1993). Mondor's disease is described as superficial thrombophlebitis of the subcutaneous veins of the chest, showing a comparable cord on the chest wall (Conant *et al*., 1993). The majority of studies on AWS imply a link to the lymphatic rather than the vascular system (Leduc *et al*., 2009; Bergmann *et al*., 2012). Apart from blood vessels and lymphatics, one author posited that the cord in the case of Mondor's disease could be the result of twisted fascia (Salmon, Berry & Hamelin, 2009). However, there still remains much uncertainty around the topic as not much clear evidence, such as biopsies of the cord, exists to show its composition (Josenhans, 2007).

Due to the cord's similar appearance in both disorders, the aetiological findings in Mondor's disease could be extrapolated to the anatomical pathology of AWS. The superficial lymphatics and vessels, which are suggested to make up the cord, are bound and anchored by superficial fascia. A fibrosed cord, as seen in both, could therefore be related and adhere to the surrounding fascial planes. Salmon and colleagues (2009) go as far as to hypothesise that the interplay of fascia might play a bigger role in the initiation of Mondor's disease than the lymphatic system does. Only Fourie & Robb (2009) suggest a possible link of damaged fasciae to AWS symptoms. Other research denies observing any involvement of fascia using imaging modalities (Leduc *et al*., 2009, 2014; Koehler, 2013; Koehler *et al.*, 2014).

1.2.3. Imaging of AWS

Medical imaging modalities allow observation of internal structures in patients. Most AWS studies have, however, focused on physical examinations of the anatomy of the syndrome (Leduc *et al.*, 2009; Fourie & Robb, 2009). In total, there have been four studies that have used ultrasound (US) imaging as an attempt to observe the cord's anatomy in AWS. O'Toole and colleagues (2015) showed linear, continuous structures which extended into the biceps brachii muscle in longitudinal direction to the cord with a "honeycomb" appearance in transverse direction, but concluded not to be able to find consistent indicators of the cord on US.

Koehler *et al.* (2013, 2014) came to a similar conclusion, as the cord could not be observed and showed no significant differences in skin thickness or echo density of the affected versus the non-affected arm in patients with AWS. A comparison to findings on Mondor's disease were made where a tubular, reduced echoic structures was observed with no flow on Doppler US (Yanik *et al.*, 2003). Although a high-frequency probe was used for increased visibility, only transverse scans were taken, giving a limited and discontinuous view.

Wei and colleagues (2013) showed a hyperechogenic tube on longitudinal B-type US which was revealed to be a blood vessel on Doppler ultrasound and thought to be the cord. Unfortunately, the findings of the study were not well explained, and the observed structure could be a regular blood vessel instead of the cord.

Leduc and colleagues (2014) provide the only study that reports the ability to visualise the cord and relating US and MRI findings, using a specific method to maintain the cord in a stretched position. Their findings show an anechoic appearance with hyperechogenic edge superficial to, or at, the hypodermis-deep fascia junction. The authors report that there was, however, no evidence of fascia involvement or focal fascial thickening.

Imaging of the cord, its contents and its relationship to the surrounding structures has thus not yet provided definitive answers about the anatomy of AWS but requires further investigation and may explain symptom onset and resolutions.

1.2.4. Onset and resolution of the symptoms of AWS

The onset of the symptoms of AWS has been found to occur between one and five weeks after the surgical procedure (Lacomba *et al*., 2009; Leduc *et al*., 2009; Cheville & Tchou, 2007; Fourie & Robb, 2009). The medical literature asserts that AWS is self-limiting and spontaneously resolves within three months (Moskovitz *et al*., 2001; Leidenius *et al*., 2003). Physiotherapists, on the contrary, suggest that when AWS is left untreated, morbidity and pain can persist for years (Kepics, 2007). In agreement with Kepics (2007), the current study notes that the same original information is reproduced and original sources are referred to in the literature without critical appraisal. Perpetuated long term-effects of AWS may thus occur when the symptoms have gone unnoticed. Long-term complications might include altered shoulder dynamics as found in many other breast cancer patients (Shamley *et al*., 2007) as well as posture problems, muscle imbalances and chronic pain (Koehler, 2013). Cheville and Tchou (2007) assert that it is the prolonged symptoms that are the biggest threat for AWS sufferers.

More studies find that patients may present with the symptoms of AWS after the three month "cut-off" suggested by the medical research and that some patients even present with symptoms three years post-surgery (Kepics, 2007; Wyrick, Waltke & Ng, 2006). Furthermore, some symptoms might disappear naturally while others require physical treatment to resolve.

1.2.5. Treatment of AWS

Several case studies have shown that manual therapies that target the soft tissues including the fasciae are beneficial in treating the symptoms of AWS (Kepics, 2007; Moreau *et al*., 2010; Fourie & Robb, 2009; Tilley, Thomas-MacLean & Kwan, 2009). Pain and shoulder ROM are found to be often be returned to premorbid states and the cord can be resolved. The therapies, however, differ substantially from each other. Whereas Fourie & Robb (2009) used tissue gliding, mobilisation and stretching as primary techniques, Kepics (2007) used cord stretching and heating and cooling techniques to work on the limited movement of the shoulder. Fourie & Robb (2009) described a "popping" sound when the cord gave way after stretching it in a longitudinal direction. The stretch led to an immediate improvement of the ROM in, especially, abduction of the arm and did not appear to have any negative consequences.

Moreau *et al*. (2010) attempted to test the efficacy of two different treatments: one focused on light work with prevention of pain; the other was more painful and utilised more stretching. They came to the conclusion that there was no statistically significant difference between the two treatments. AWS treatments in the literature seem to have some overlap focusing predominantly on the myofasciae, but the effectiveness of particular treatments and which are the most effective remains unclear. Davies & Logan (2010), for example, observed reoccurrences of the cord in two of their patients after their treatment protocol. The ambiguous results of the treatments reported in the literature show that a more standardised and generalised treatment plan is needed for patients suffering from AWS.

1.2.6. Gap in the AWS literature

The burden of AWS is often underestimated by health professionals (Josenhans, 2007) but it is unknown whether they undervalue the problem because of (i) the unclear definition of what constitutes the disorder, (ii) belief that it is self-limiting or (iii) uncertainty regarding its aetiology. Education and improved knowledge of the disorder are essential. Current research lacks a focus on the anatomical structures associated with the symptoms as the functional anatomy may explain more about the aetiology of the syndrome.

A possible role of fascia in the development of the cord and other symptoms is likely because of the cord's adhesive presentation, its likelihood to be a superficial vascular structure and hence its continuity with the surrounding fascia. Fascia, as a previously unexplored area in AWS imaging research, may thus provide new insights into the aetiology of the disorder. US imaging was shown to reveal fascial differences clearly (Paulssen & Shamley, 2012 [unpublished academic mini-dissertation]). Manual treatments have been used to treat the symptoms of patients but require standardisation and need to be guided by anatomical evidence. Monitoring manual treatment and the observation of the structural changes via imaging modalities may thus help determine the role of the different anatomical structures, including the fasciae, in relation to the syndrome.

1.3. Study relevance

The relevance of the current research project lies with its contribution to the literature on AWS that is generally very limited, unclear and that can be contradictory, and that contains little previous research on establishing the occurrence of the syndrome in the South African context. The current study builds on existing research but adds new perspectives to a field that has confined itself to understanding the cord's origins rather than understanding the source of the symptomology experienced by the patients. The present study is one of the first studies to consider fascia as a contributing factor to the symptoms in AWS and one of very few studies that uses both an internal and external approach to determine the anatomical characteristics of the syndrome. By using ultrasound imaging before and after physiotherapy that focuses on the fasciae, observed changes in symptomology may be explained by changes on the scans. Furthermore, a more complete picture of the syndrome is created because of the increased number of clinical and demographic variables that are analysed compared to recent studies and because of imaging data which give information on the structures involved and could help guide future treatments (Wyrick, Waltke & Ng, 2006; Moskovitz et al., 2001; Davies & Logan, 2010).

1.4. Purpose of the study

From the literature, a flow diagram on how fascia could contribute to AWS symptomology was constructed that aided in the design of the current project (see Appendix A). To investigate the relationship between fascia and AWS symptoms, the study attempts to address two hypotheses and three aims:

<u>Hypothesis 1</u>

Altered fascia plays a role in the restriction of upper limb movement, the perpetuation of pain and the fibrosis and formation of the cord in axillary web syndrome (AWS).

Aim 1

To descriptively relate variables that were found to be (risk) factors in AWS literature to our study and the fascia literature to determine fascial involvement.

I. To obtain demographic and clinical variables from patient records.
II. To descriptively correlate and describe the outcome measures described under the Aim 2.

Aim 2

To test the use of ultrasound (US) as an imaging technique for fascia in AWS in patients after treatment for breast cancer and to observe whether findings on the ultrasonographs relate to the presenting symptoms complex.

Objectives

I. To determine the anatomical structures involved in AWS through:
    - **External observation**, i.e. photography of the cord, measurement of the cord length and localisation of the cord.
    - **Internal observation**, i.e. ultrasound (US) and magnetic resonance imaging (MRI).
II. To measure the range of movement (ROM) manually via a goniometer.
III. To measure shoulder pain and disability using the Shoulder Pain and Disability Index (SPADI) and determine more localised tissue tightness and pain.
IV. To determine quality of life using the FACT-B questionnaire.
V. To descriptively correlate and describe the outcome measures described above.
VI. To compare and contrast the observed morphological characteristics between the different patients in the area of interest (the axilla).
VII. To determine cord presentation in terms of patterns and variations.

<u>Hypothesis 2</u>

Changes on US images of the cord, fascia and surrounding structures will be evident when the cord resolves, or symptoms improve.

Aim 3

To determine whether changes in fascia on US images can be seen after manual therapy and to descriptively relate the US findings to possible changes in the other outcome measures.

Objectives

I. To evaluate and obtain outcome measures as described for the first aim over time at two specific points: **before** and **after** the manual treatment.

Chapter 2: Literature Review

To understand the possible involvement of fascia to the symptomology of the patients in axillary web syndrome (AWS), an overview of the general fascia literature and the fasciae and structures in the anatomical area of interest, the axilla, are described in the following chapter.

2.1. Introduction

Although recent human anatomical research has largely focused on applied anatomy, the fasciae as a connective tissue network still remains to be described in detail (Schleip, 2006). Its omission from most anatomy atlases shows that the tissues that the fascia encompasses, of which still little is known, have not been considered as vitally important (Schleip, 2009). In both educational and research spaces the tendency has been to remove the fascia in order to uncover the muscles or the organs being investigated, possibly because it was thought not to have a clear function, but also because it can be a difficult tissue to understand and research (Guimberteau & Armstrong, 2015). New technologies such as ultrasound (US), magnetic resonance imaging (MRI) and endoscopy make researching the fasciae easier (Langevin & Kawakami, 2012; Guimberteau & Armstrong, 2015). Current efforts by numerous researchers to explore the fasciae are adding to an expanding field that may aid in understanding diseases that before could not be explained (Van der Wal, 2012; Stecco, 2015,). AWS may be one such disorder, and to understand the underlying structural changes that have occurred in the syndrome, the basic anatomy of the axilla and its contents are described.

2.2. The anatomy of the axilla

Stecco (2015) describes the axilla as a pyramidal-shaped cavity that lies between the upper limb and the upper part of the lateral thoracic wall. Due to its central position between the two parts, it plays an important role in upper limb movement. Many force lines extend through it from the different muscles forming its borders and that act on the shoulder joint. The anterior border of the cavity is shaped by pectoralis major and minor and the posterior wall by subscapularis superiorly and latissimus dorsi and teres major inferiorly. A medial border is lined by the intercostals of ribs 1-4 and serratus anterior forming an arched wall with the lateral wall being shaped by the conjoining of the anterior and posterior wall. Its inlet is continuous with the neck superiorly and allows for passage of major vessels and nerves through it to and from the upper limb. Its contents include the infraclavicular part of the brachial plexus that supplies the upper limb, numerous lymph nodes important in cancer metastases, and vessels such as the axillary artery and vein, fibrofatty tissue and it may contain the axillary tail of the breast (a continuation of the mammary glandular tissue) entering it (Standring, 2008). Enveloping and connecting all the structures is the fascia.

2.3. Fascia

The fascia, or "band" in Latin, is described in *Gray's Anatomy* as "masses of connective tissue that are large enough to be visible to the unaided eye" (Standring, 2008). The *Terminologica Anatomica* describes it as a "sheath, sheet or any dissectible aggregate of connective tissue" (Stecco, 2015). A more recent definition was proposed at one of the first Fascia Research Congresses to incorporate all connective tissue structures and avoid excluding some due to "dissective" anatomical terminology (Findley, 2007) as the fascia is a continuous structure rather than comprising independent parts. Fascia was described as the "soft tissue component of the connective tissue system that permeates the human body" (Schleip, Jäger & Klinger, 2012). It includes not only the fascia underneath the skin (superficial fascia) or enveloping muscles (deep fascia) and organs (visceral fascia), but extends to incorporate ligaments, tendons and regionally specialised tissues such as the "flat tendons" or aponeuroses. The fascia is seen as a three-dimensional network that spreads throughout the whole body, connects to all tissues and has different macroscopic and microscopic features depending on the location in which it is found (Abu-Hijleh *et al.,* 2006; Stecco & Stecco, 2012).

2.3.1. Components

Microscopically, fascia consists of fibroblast cells, collagen and elastic fibres and extracellular matrix (ECM) (Stecco, 2015). The fibroblast cells allow the tissue to be metabolically active whereas the fibres are responsible for the mechanics and the ECM provides malleability (Stecco, 2015). The ECM forms the scaffold for cells and contains ground substance containing water, extracellular proteins, glycosaminoglycans, proteoglycans and collagen and elastic fibres (Williams, Holleman & Simel, 1995). Collagen has the highest tensile strength whereas elastic fibres provide distensibility (Stecco, 2015). The fibres form fascial fibrils with irregular microvacuolar polyhedral shapes which differ in appearance depending on the different types of fascia (Figure 2.1) (Guimberteau & Armstrong, 2015).

Figure 2.1. *The fibril composition of the fasciae. Photo courtesy of Jean-Claude Guimberteau, 2015.*

2.3.2. Classifications

The fasciae are of the subtype connective tissue proper and can be found to be loose or dense.

Loose connective tissue, sometimes called areolar tissue, is the most abundant in the body with an increased amount of ECM and the preponderance of adipocytes (Benjamin, 2009). The collagen in loose connective tissue is dispersed multi-directionally, offering a framework in which the adipocytes are interspersed (Stecco, 2015). Its components make it a gel-like tissue (Day, Stecco & Stecco, 2009). It is found in the hypodermis of the skin but also between muscles and organs, and allows for independent movement by providing a gliding surface to reduce friction between neighbouring planes (Stecco *et al.*, 2006; Stecco *et al.*, 2011).

The dense connective tissue contains much stronger and organised collagen and is packed very densely with few cells (Stecco, 2015). Dense connective tissue, due to its highly structured architecture, is able to resist mechanical stressors put on it (Day, Stecco & Stecco, 2009; Huijing, 2003). Several different types are classified: dense irregular connective tissue is found within the dermis and as part of the superficial fascia, and dense regular connective tissue that makes up the deep fascia, visceral fascia, tendons and ligaments (Schleip, Jäger & Klinger, 2012).

It is important to note that, contrary to anatomical thinking, the fascial tissues are not distinct entities but more regional specialisations and are continuous with one another throughout the body (Guimberteau & Armstrong, 2015). Figure 2.2 illustrates the body-wide three-dimensional connective tissue network of the fasciae connecting skin to bone. The different subsections of fascia are discussed in the next section.

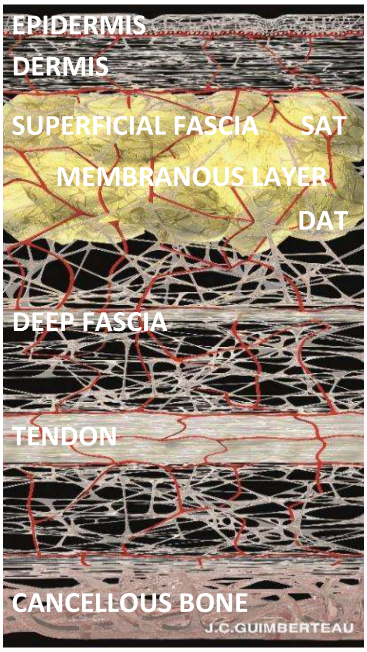


Figure 2.2. *A cross-sectional schematic of the fasciae from epidermis to cancellous bone. The independent components of the superficial fascia are not shown but are instead highlighted. DAT=deep adipose tissue, SAT=superficial adipose tissue. Schematic adapted from Jean-Claude Guimberteau, 2015.*

2.3.3. Superficial fascia

The first clear layer of the fascial system, called the superficial fascia (SF) or hypodermis, is located below the dermis and epidermis, which contains a dense network of connective tissue, and comprises different sublayers with a clear structure (Lancerotto *et al.*, 2011).

Anatomical research using cadaveric dissections revealed that the superficial fascia has a membranous layer with sometimes multiple lamina, which may be found within the tissue with a layer of adipose tissue superficial to it (superficial adipose tissue or SAT) and below it (deep adipose tissue or DAT) (Figures 2.2 and 2.3a) (Stecco *et al*., 2009; Chopra *et al*., 2011). The membranous layer sprouts off different fibrous septa or skin ligaments that connect to the dermis (retinaculum cutis superficialis) and to the deep fascia of the muscle (retinaculum cutis profundis) providing a physical link (Figure 2.3b) (Stecco & Stecco, 2012). Surgically, however, it appears to blend with its skin ligaments and may not be a distinct layer (Guimberteau & Armstrong, 2015). Guimberteau and Armstrong (2015) suggest that the layer should rather be seen as a reinforcement of the fascia fibrils. The discrepancy between the views may arise from the methodology of dissecting an embalmed and dehydrated structure in cadavers versus observation in vivo during surgery (Guimberteau & Armstrong, 2015), making the tissues appear more dense than they are in a living body.

The membranous layer was previously thought to be confined to the abdominal wall exclusively, but has since recently been shown by several authors to be present all around in the body (Abu-Hijleh *et al*., 2006; Chopra *et al*., 2011) in different appearances. The thickness of the layer is dependent on the location within the body (thicker in the lower limb than upper limb), the anatomical position (posteriorly thicker than anteriorly) and on the sex of the individual (thicker in women than in men) (Huerta & García, 2007). The adipose content of the SF depends on climate (higher in colder climates), body habitus (increased in obese individuals) and sex (increased in women) (Standring, 2008). The skin ligaments themselves can be absent or very prominent or a more fibrous or fatty appearance may be found (Stecco & Stecco, 2012). The appearance relates to the functional mobility the tissues require – fewer and longer skin ligaments are found in areas that require increased mobility, for example, providing the ability of the dermis and SF to move independently over the muscle (Stecco & Stecco, 2012).

Functionally, as the SF layers comprise mainly elastic fibres it allows, together with its extensions to the dermis, for continuous endogenous tension onto the dermis (Standring, 2008). The so-called Langer's lines or skin tension lines provide tissue memory permitting the skin upon stretch to return to its original shape (Crumpler & Ghaudhry, 2001; Borges & Alexander, 1962). Aging decreases the elastic abilities of the tissues which is a proposed reason for the development of wrinkles (Abu-Hijleh, Dharap & Harris, 2012). SF also provides a framework for vessels (Figure 2.3c), lymphatic vessels (Figure 2.3d) and nerves which it invests in (Standring, 2008). The framework is particularly important in aiding to ensure that veins are kept patent.

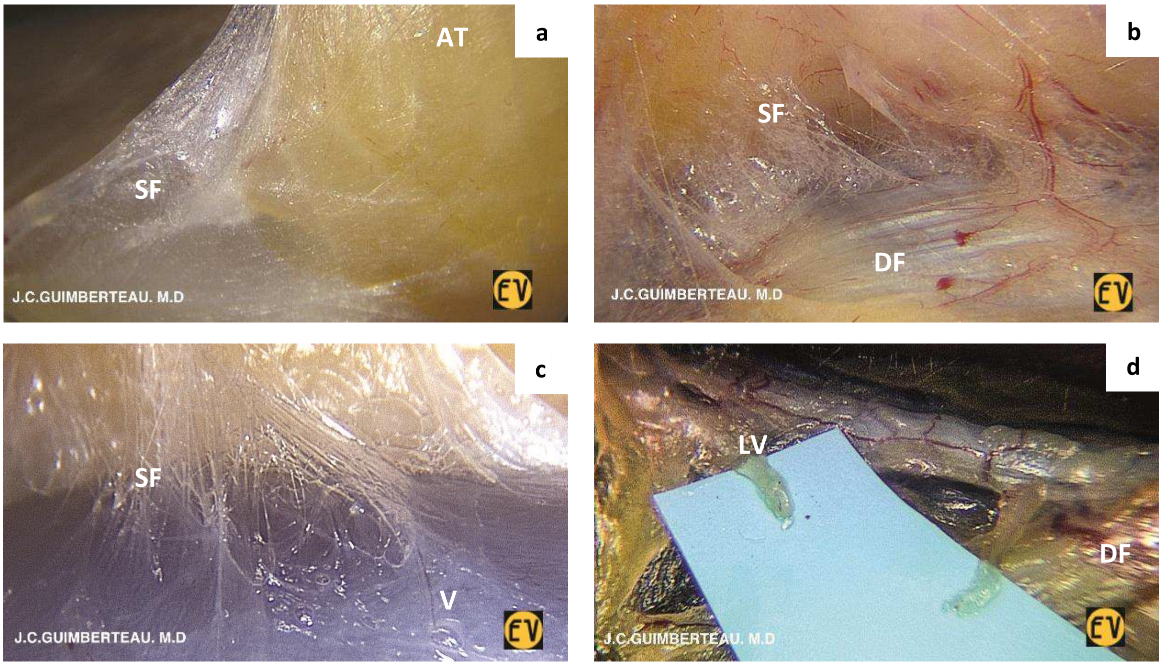


Figure 2.3. *Fascia investing in different tissues. (a) The framework of the superficial fascia investing into the adipose tissue, (b) the close connection of the superficial fascia to the deep fascia, (c) investing fascia into the wall of a vein, (d) fascia surrounding the lymphatic vessels, shown on the blue paper. AT=adipose tissue, DF=deep fascia, LV=lymphatic vessel, SF=superficial fascia, V=vein. Photos courtesy of Jean-Claude Guimberteau, 2015.*

The vessels and nerves are located in different parts of the SF as explained by Stecco (2015). The arteries run both perpendicularly and longitudinally to the dermis forming networks or plexi in the SAT and membranous layer. Communicating veins that transverse the different layers are predominantly present in the SAT and DAT connecting to horizontal veins in the membranous layer. The lymphatic veins form plexi close to the skin and send off shoots along the skin ligaments as they have thin walls and require support, then anastomose within the membranous layer to the bigger vessels running in the DAT where lymph glands are also located. Nerves form small plexi close to the skin which connect to Ruffini and Pacini corpuscles in the SAT and membranous layer of the SF and respond to stretch and compression respectively. They connect to bigger nerves in the DAT which run obliquely to reduce shearing force on them, preventing damage. The different layers also contain many free nerve endings responsible for sensing pain (Myers & Frederick, 2012).

The general features described above are more specifically adapted in the fascia of the breast, axilla, upper limb and shoulder.

2.3.3.1. The superficial fascia of the breast, axilla, upper limb and shoulder

The superficial fascia (SF) of the thorax is continuous with the superficial fasciae of the breast, axilla, upper limb and shoulder (Stecco & Stecco, 2012). Dissection of the breast in a woman highlights a continuous layer of membranous fascia within the superficial fascia encompassing the mammary gland (Stecco, 2015). The axillary fascia results from the junction of the superficial fascia of the thorax, upper limb and back and unites with the surrounding muscles' deep fasciae (Stecco & Stecco, 2012). The SF in the axilla contains holes that contain fibrofatty tissue which allow vessels and nerves to pass through (Standring, 2008). The DAT lying within the cone of the axilla is especially clear in patients with higher BMIs (Stecco, 2015). Stecco and Stecco (2012) furthermore describes that the SAT and DAT of the upper limb and shoulder have less adipose tissue making the SF a thinner structure there. At bony points and others, such as at the inferior border of the deltoid muscle, the superficial fascia also merges with the deep fascia forming anatomical compartments (Stecco, 2015).

2.3.4. Deep fascia

Compared to its superficial counterpart, the deep fascia is closely connected to the musculature which is called myofascial continuity (Gautschi, 2012) (Figure 2.4a). The deep fascia is described as consisting of organised, dense layers (Benetazzo *et al.*, 2011). The deep fascia also includes the aponeurotic fasciae that forms thickened sheaths into which muscles can insert via myofascial expansions and shape anatomical compartments (Figure 2.5a), and is related to providing strength and resisting force (Stecco, 2015). It also includes the epimysial fascia which envelops individual muscles and interacts with their fascicles closely (Stecco, 2015) (Figure 2.4b). The close connections to muscular tissue highlights an important role of the tissue in the biomechanics of the musculoskeletal system (Fourie, 2012), comprising the bones, muscles and fasciae extending into both.

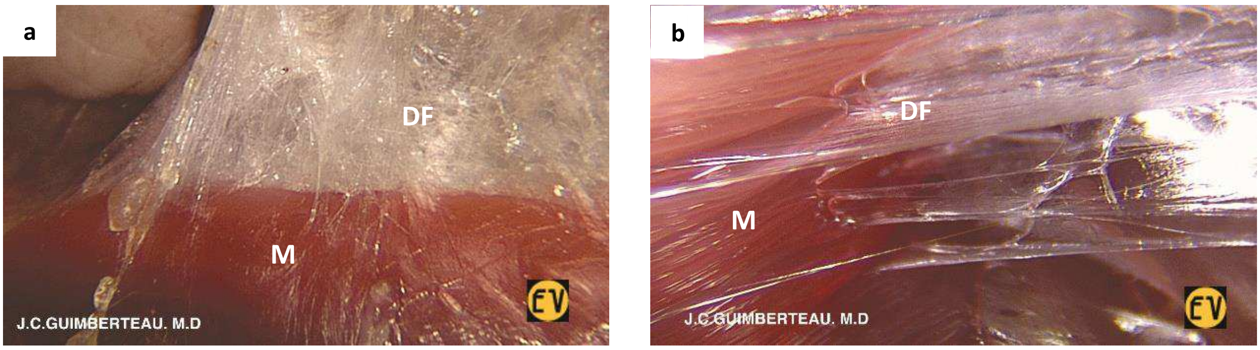


Figure 2.4. *Fascia investing in muscle. (a) The deep fascia investing closely to the muscle, (b) the deep fascia extending between the muscle fibres forming the perimysium. SF=superficial fascia, DF=deep fascia, M=muscle. Photos courtesy of Jean-Claude Guimberteau, 2015.*

On a smaller level, the perimysium separates the different muscle bundles or fascicles (Figure 2.4) which connect to the endomysium, which in turn, divides each bundle into muscle fibres (Stecco, 2015; Guimberteau & Armstrong, 2015). Whereas the endomysium is thought to be more involved with metabolic control and smooth gliding, the perimysium is involved with force transmission and is part of the epimysial fascia (Purslow, 2010; Stecco, 2015).

The mechanical abilities of the deep fascia are dependent on the stiffness of the tissue. The stiffness, resulting from ECM composition, leads to other biomechanical properties such as force resistance to force and load (Schleip, Jäger & Klinger, 2012). Increased collagen content makes the tissue more resilient to forces (Guimberteau, 2012). How the fascia may adapt to force load is also subject to the smooth gliding between different layers and the collagen alignment (Oschman, 2012). Depending on the location in the body, the tissues present with different layering (Stecco, 2015). Aponeuroses, consisting of multiple layers that are aligned in different directions, appear to be able to resist force in multiple directions (Langevin *et al*., 2009). Between each layer one can find areolar tissue or a layer of hyaluronan, a lubricant produced by hyaluronan-producing cells of fibroblast lineage, both of which allow for smooth movement and reduced friction (McCombe, 2012). The lubricated layer is also present between the muscle and the epimysial layer and between each collagen fibre.

Smooth limb movement is an interplay of muscle contraction and relaxation which is regulated by deep fascia receptors called muscle spindles (Fourie, 2012). The muscles spindles provide proprioceptive information to the central nervous system on the state of muscle contraction and positioning of the body (Stecco, 2015). Activation of the muscle spindles due to the stretching of the epimysial fascia and DAT results in reduced muscle activation to prevent overexertion (Stecco *et al*., 2009a). The fascia is then able to modulate muscle activity responsible for controlling quality of movement (Fourie, 2012). As muscles or portions of muscles are activated, specific areas of the deep fascia are stretched which together with nerve receptors allow for mutual feedback between the two tissues (Stecco, 2015).

2.3.4.1. The deep fascia of the breast, axilla, upper limb and shoulder

The deep fascia of the trunk consists of three laminae of connective tissue that provide independent gliding planes for the different muscles they envelop, but form an anatomical continuity (Figure 2.5) (Stecco, 2015). The myofascial layers are: the thickest, superficial lamina that surrounds pectoralis major below the mammary gland, latissimus dorsi and surrounds sternocleidomastoid and trapezius posteriorly; the middle layer that envelops the pectoralis minor, serratus anterior and extends to the back and abdomen; and the deep layer which incorporates mostly intercostal and abdominal muscles before it extends to the back.

The superficial lamina over the pectoralis major is its fascia, which is sometimes removed but most often damaged during mastectomies (Lacomba *et al*., 2010; Fourie, 2008), and sends multiple fibrous septa into the muscle between the different muscular fibres (Stecco *et al.*, 2009a). Stecco (2015) describes that the pectoralis major fascia consists of two layers and attaches laterally to the deltoid fascia and axillary fascia after it continues to become brachial fascia. Over serratus anterior the double-layered structure becomes one, but remains bilayered to encompass latissimus dorsi posteriorly where it also envelops deltoid. Medially, the superficial layer is continuous with the contralateral pectoralis fascia whereas the deep layer invests into the sternum. The superficial layer has expansions that extend towards the brachial fascia and form lines of force.

The axillary fascia connects to the superficial lamina and has a cone shape (Stecco, 2015; Standring, 2008). It is continuous with the brachial fascia towards the upper limb, serratus anterior medially and posteriorly with the latissimus dorsi. Multiple connections exist between the shoulder girdle and axillary fascia, resulting in many different force lines acting on it, forming the oval window (see Figure 2.5c) (Stecco, 2015).

The middle lamina of the deep fascia of the trunk forms the clavipectoral fascia that envelops predominantly pectoralis minor but becomes the axillary suspensory ligament (Figure 2.5d). The structure allows the axillary contents to be lifted up upon arm movement (Stecco, 2015). It also forms a costocoracoid ligament that isolates the axillary cavity from the thorax anteriorly.

The deep lamina incorporates serratus anterior, subscapularis and subclavius. At the shoulder joint the three lamina join with the subdeltoid bursa and posterior part of glenohumeral joint (Stecco, 2015).

2.4. Biotensegrity and fibrillar chaos

To understand the global biomechanical consequences of a continuous system in the mobile axilla highlighted in the sections above, one can refer to the concept of biotensegrity. Biotensegrity applies the architectural term "tensegrity" to the human body (Chaitow, 2014). Tensegrity, a combination of the words tension and integrity, has the premise that a structure consisting of separate elements can exist with the elements not touching one another due to their connection to elastic continuously tensed elements (Levin & Martin, 2012). The link provides a tension-compression system that can resist forces by transmitting and redistributing the forces (Levin & Martin, 2012). In the context of the human body, tensegrity explains that the skeleton is not the main scaffold but rather is suspended within the fascia (Chaitow, 2014).

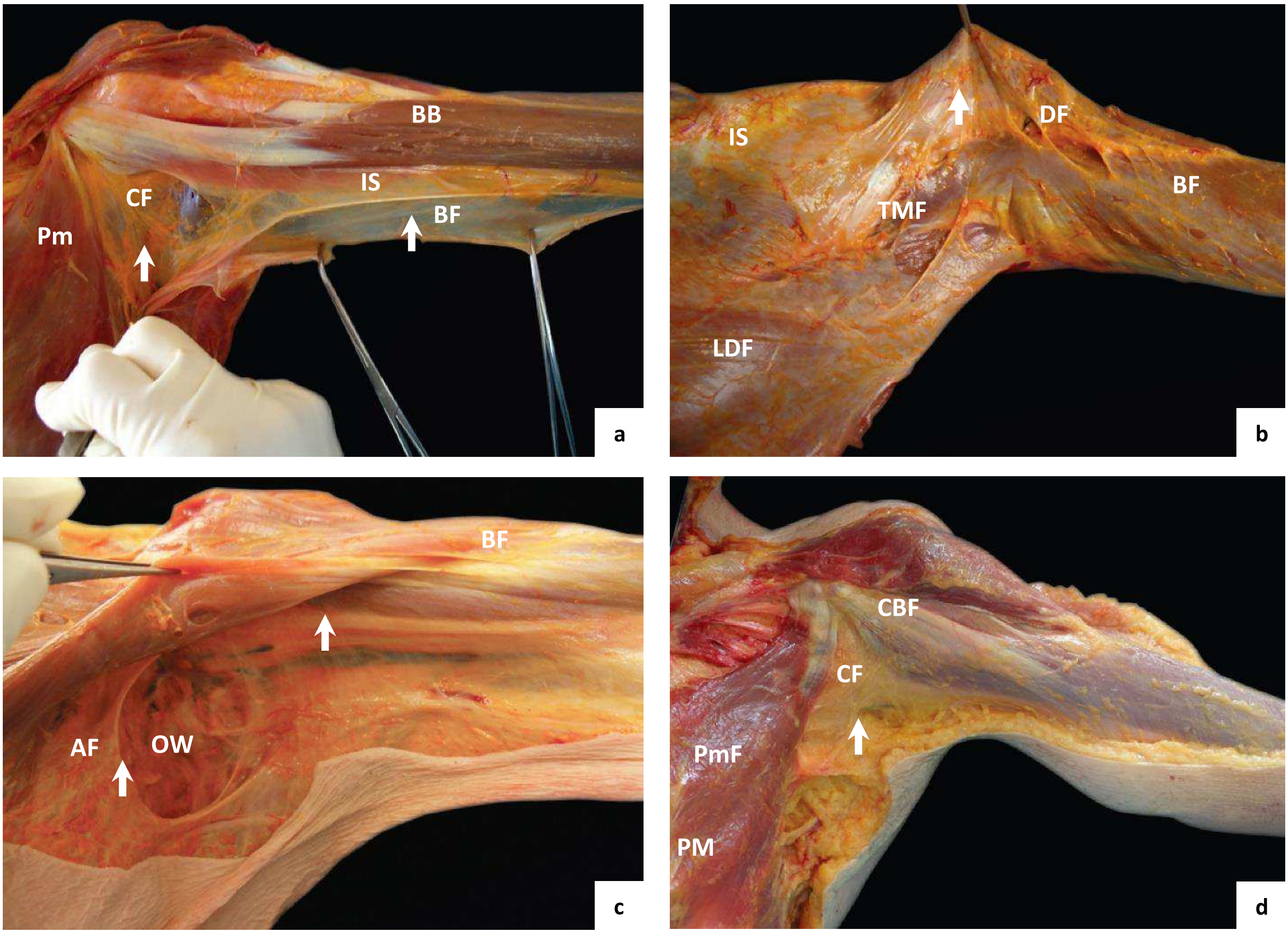


Figure 2.5. *Fascial anatomy of the shoulder girdle and axilla. (a) The continuity of the fascia and the myofascial insertions into the muscles (see arrows). (b) The posterior aspect of the arm and the continuity of the fascia overlying the muscles (see arrow). (c) The oval window in the axilla formed by the different fasciae meeting there and the fibrofatty tissue inside the axilla. The arrows denote the different fascial directions forming the window. (d) The undissected axilla with the clavipectoral fascia extending towards it forming the suspensory ligament (see arrow). Note the continuation of the fascia over coracobrachialis. AF=axillary fascia, BB=biceps brachii, BF=brachial fascia, CB=coracobrachialis, CF=clavipectoral fascia, DF=deltoid fascia, IS=intermuscular septum, LDF=lattismus dorsi fascia, OW=oval window, Pm=pectoralis minor, PmF=pectoralis minor fascia, PM=pectoralis major, TMF=teres major fascia.*

Photos courtesy of Carla Stecco, 2015.

Further evidence for the biotensegrity system in the human body is highlighted by Guimberteau and Armstrong's visualisation of the fascia on a mesoscopic level.

Using endoscopic intratissular videophotography, the fascia is highlighted as a chaos of fibrils that are able, due to their dynamic ability, to split from one another and re-attach, with its web-like architecture to act as a shock-absorber (Guimberteau, 2015). Furthermore, they can resist forces by dissipating and transferring them over distance (Guimberteau, 2015) (Figure 2.2).

2.5. Remodelling and the inflammatory response

Tensional forces across the tissue not only provide it its shape, but also aid in remodelling and restoring the tissue to its original mould when damaged (Fourie, 2012; Guimberteau, 2015). The fibroblasts that produce the ECM and fibres are involved with remodelling the tissues in response to physical demands (Purslow, 2010). According to Wolff's law, bone is remodelled in the direction of force put on it (Oschman, 2012). The remodelling reaction is also observed in fascia where collagen fibres are realigned in the direction of force (Oschman, 2012). Remodelling avoids a compressive load on the fascia and strengthens the fascia in that direction (Levin & Martin, 2012), dynamically adapting to the situation.

Upon tissue injury, i.e. when tissue integrity is lost, a wound-healing cascade is activated in which inflammatory cytokines are released and inflammation occurs (Van den Berg, 2012). More fibre-producing fibroblasts then enter the tissues to produce granulation tissue and changes to the ECM occur. Granulation tissue consists of a weaker form of collagen (type III) but which gets replaced with a stronger type I collagen as the scar matures (Van den Berg, 2012). Some fibroblasts then specialise to myofibroblasts which can contract and aid in closure of the wound (Van den Berg, 2012) in response to the tension force lines on the tissue. The ability of the skin to restore integrity under non-pathological circumstances via the wound-healing cascade is important for it to regain its original form and tension, although the tissue quality will be reduced (Fourie, 2008).

Chronic inflammation can, however, occur as a result of too much damage or if the tissue is irritated continuously during the healing process. Fibrosis, or the excessive deposition of collagen under the influence of TGF-B, is laid down haphazardly as a means to restore tissue integrity in the form of a scar (Fourie, 2012). Furthermore, neighbouring tissues can also become affected due to the widespread cytokine release leading to changes beyond the original insult.

2.6. Pathology and functional consequences

The consequences of chronic inflammation are manifold and can result in both structural changes and functional limitations. In terms of structural alterations, Stecco (2015) makes a differentiation between fibrosis and densification. Fibrosis is the laying down of excess collagen in a haphazard way in a pathological situation as a result of chronic wound-healing such as in a scar. Fibrosis may be visualised on imaging by an increase in echogenicity on US (Langevin *et al.*, 2009). On the other hand, densification is explained as any change in the composition of the loose connective tissue components including adipose tissue, glycosaminoglycans and hyularonan (Stecco, 2015).

Structural changes such as those resulting from repetitive stress injuries, strain and over-use can lead to alterations in the viscosity of the fascia. ECM is replaced, making the tissue stiffer and the ability of the fascia to absorb stressors is diminished (Stecco & Stecco, 2012). Fibrosis, when ECM has become replaced by rigid collagenous tissue, may show a similar effect. Furthermore, a stiffer tissue does not permit regular stretch of the spindles, which has been hypothesised to lead to an inability of certain muscle parts to be activated, affecting joint movement and causing pain (Stecco, 2015). Conversely, stretching of the myofascial expansions linking to a thickened epimysial fascia can lead to chronic activation of the spindles and subsequent muscles which are in a continuously contracted state leading to joint impairments and pain (Stecco, 2015). Furthermore, chronic contraction can lead to antagonistic and synergistic imbalances in movement and proprioception (Stecco *et al.*, 2009b).

Adhesions, or the adhering of two planes of tissue, may occur when damaged tissue is further irritated after initial healing (Fourie, 2008). Adhesions may cause pathological force lines in the fasciae and affecting strain on other tissues. Due to the continuity of the system explained by biotensegrity (Gautschi, 2012), adhesions may have body-wide consequences. Myofascial trigger points (MTPs) are localised areas of muscle tightening, with fascial shortening and adhesive cross-links (Gautschi, 2012). Any fibrotic change, as seen in MTPs to fascial layers, has been hypothesised to lead to ischeamia (Distler, 2007). As a result, fascial scars and taut bands develop within the deep fascia that lead to restricted movement (Gautshi, 2012). Restricted mobility can lead to poor posture and resultant strain on muscles and joints via force lines in the affected area.

Furthermore, adhesion between multiple fascial layers can prevent smooth movement upon normal stretch or muscle contraction and lead to the overactivation of nociceptors and resultant pathological symptoms such as pain (Gautshi, 2012). Abnormal changes, such as adhesions, may be visualised using imaging modalities.

2.7. Fascial imaging

Many different imaging techniques have been used to visualise fascia. However, fasciae are not typically examined by radiologists and hence there is limited research that describes normal and abnormal fasciae on imaging modalities (Langevin & Kawakami, 2012). Normal fascia on CT scans shows hyperdense layers and hypodense adipose tissue (Ozturk *et al*., 2012). On MRI, normal fascia shows both hypodense signals on T1- and T2-weighted imaging (Langevin & Kawakami, 2012) and adipose tissue is enhanced (Stecco *et al*., 2014). On ultrasound (US), the fascia presents as echogenic lines and fractions with hypoechoic layers of adipose tissue (Langevin *et al*., 2009). Although CT and MRI can show the location of the different planes more easily, US gives more structural detail permitting the researcher to measure structural features (Langevin & Kawakami, 2012). Furthermore, US is cost-effective and is able to show tissues moving dynamically (Leduc *et al*., 2014). Dynamic observation allows the analysis of tissue glide as shown in a study by Langevin and colleagues (2011). Some researchers favour US over MRI because of the ability of US to distinguish better between tissues containing a fibrous component such as in fibromas (McNally & Shetty, 2010). The major limitation of US imaging is the operator's skill and experience in utilising the technique (Luomala *et al.*, 2014). In addition, a requirement to analyse fascia is a full understanding of its structure and any abnormalities related to it (Stecco, 2015).

2.8. Fascial abnormalities on US imaging

Several studies that use US have shown fascia abnormalities to be implicated in pathology. Findley (2012) describes a case where fascia continuity was disrupted in the abdominal fascia in a car accident with continued pain in the area years later. Langevin and colleagues (2009; 2011) showed in two subsequent studies fascial thickening on US and, using gliding potential analysis, that there was less shear strain, indicating an inability for smooth fascial glide in patients with lower back pain, possibly leading to the symptoms. Wearing (2012) describes thickened plantar facia in plantar fasciitis, correlating to collagen degeneration and fibre disorientation. Chronic contraction of muscle can lead to all the findings (Myers & Frederick, 2012).

Day and colleagues (2009) found in their study of chronic neck pain that there was increased fascial thickness which correlated to reduced smooth movement, affecting ROM of the muscles and pain. The authors hypothesised that the symptoms are caused by an increase in the density of the hyaluronic acid which results in stiffness. Axillary fascia has been thought to become densified in overuse syndromes of the shoulder (Stecco, 2015). Changes in hyaluronic acid in another study were found to possibly contribute to pain, inflammation and loss of function (Lee & Spicer, 2000).

Apart from visualising the structural and functional anatomy, the non-invasive imaging modalities are able to give specific direction to treatment but can also monitor tissue changes during treatment (Findley, 2012). Physiotherapy treatment has been particularly effective in treating some individuals with fascial-related pathology.

2.9. Physiotherapy

Immobility and pain due to scar tissues and adhesions can be very debilitating and are often seen by physiotherapists. Furthermore, long-term immobilisation can lead to permanent movement morbidity and an inability to return to prior level of mobility (Van den Berg, 2012), e.g. as a result of shoulder joint stiffening (Schultheis *et al.*, 2012).

Tissue stiffness and mobility of the joints appear to be alleviated by manual therapies and fascial stretching. Stretching has been suggested to lead to functional changes in the abnormal tissues, causing the increased remodelling of collagen and allowing the structure to modify according to new demands (Myers & Frederick, 2012).

Another proposed mechanism to explain how the fascia becomes more fluid upon stretching is by the release of water from the ground substance changing the matrix, making the tissue more pliable and possibly altering fibroblasts and their production of collagen (Schleip, 2012; Meert, 2012). Bouffard and colleagues (2008) found that stretching scar tissue induced in mice for ten minutes twice a day, for one week, caused a decrease in both TGF-B and collagen. Other suggestions include skilful activation of mechanoreceptors that stimulates receptors that might have been stuck in fibrotic tissue in order to "re-educate" and loosen the receptors (Schleip, 2003). Deep friction, on the other hand, has been thought to improve perfusion and healing (Van den Berg, 2012). A study by Yang and colleagues (2005) showed that regular stretching of tendons had an anti-inflammatory response which also improved homeostasis of the tissues.

Adhesions and MTPs can be identified by manual palpation by a physiotherapist. Using a myofascial release technique was found to restore independent muscle gliding, improve coordination between neighbouring myofascial structures and improve fluidity of the tissues (Fourie & Robb, 2009). It also allows the therapist to break membranes that have become adherent (Bouffard *et al.*, 2008; Myers, 2012) by using shear stress on one layer to move it relative to the other. One of the few studies looking at fascia with imaging post-treatment highlighted a reduction in fascial thickness to normal levels and was shown to reduce pain and disability (Stecco *et al*., 2014*).* Manual treatment may thus be effective in modifying fascia.

From the literature one can observe that damaged, fibrotic or densified fasciae may be related to symptoms of pain and impaired movement due to anatomical or physiological restrictions. Few studies have looked at the link between symptomology and anatomy in detail and have noted specific characteristics that one can extrapolate to other diseases in which injured fascia may be implicated. Only one study used imaging to observe changes after physiotherapy treatment (Stecco & Stecco, 2012). The current study's approach to AWS, which has an obvious puckering and adhesive presentation, will describe US features and relate pre- and post-physiotherapy and affected and unaffected arm ultrasonographs. US alignment will be used to observe wider fascial involvement and to relate the patient's symptoms through methodical and limited statistical measures to establish trends.

Chapter 3: Materials and Methods

The findings of the study are reported using the *Equator Standards for Reporting* (Equator, 2013). The current study complied with the *Helsinki Declaration* (World Medical Association, 2008).

3.1. Study design

The present study is both qualitative and quantitative in nature. It is a predominantly descriptive, observational, pilot, proof-of-concept study with a case-series design that focused on the use of ultrasonography (US) to detect the fasciae in the axillae of women presenting with axillary web syndrome (AWS). The study adhered to the guidelines for the *Development and Evaluation of Randomised Control Trials for Complex Interventions to Improve Health* and was a Phase 1 study (Medical Research Council, 2000). The current study attempts to develop a greater understanding of the underlying clinical syndrome of AWS and, specifically, the anatomical structures focusing on the fasciae present on US images of the cord and surrounding tissue. Furthermore, evidence that is generated may contribute to knowledge of the therapeutic intervention in relation to the disorder (Medical Research Council, 2000).

3.2. Researcher training and consultations

The researcher obtained training to operate the US machine during his Honours degree from a doctor of anatomy who was skilled and experienced at performing US. Furthermore, training exercises to understand the anatomy of the axilla were done on peers and self to familiarise the researcher with the observations before scanning and analysis. The researcher also consulted with researchers in the field of AWS, the team physiotherapist, a radiologist regarding radiology treatment, obtained surgical advice from a professor in surgery and was guided by his supervisors who are anatomists. Furthermore, to improve insight into the treatment procedure, the researcher observed a unilateral and bilateral mastectomy with axillary clearance done in an oncology theatre at Groote Schuur Hospital.

3.3. Characteristics of the study population

The study included patients treated for breast cancer who presented with AWS (*n* = 11 patients). The inclusion and exclusion criteria are presented in Table 1.

Table 3.1. *Inclusion and exclusion criteria for patients during recruitment.*

Inclusion criteria	Exclusion criteria
Age 18 years or older	Unable or unwilling to consent
Afrikaans/English speaking	
Surgical treatment for breast cancer (uni- or bilaterally) with/without adjuvant treatment	
Presence of cording with/without pain and reduced ROM	

3.3.1. Study sites

The research study sites were the Department of Radiation Oncology at Groote Schuur Hospital (GSH) at six-month oncology check-up appointments at which patients were screened for AWS after breast cancer treatment for a total of six months, the GSH Ultrasound Unit (C10) for the first and second measurement cycle of the study and at our team physiotherapist's private physiotherapy clinic where the patients received their physiotherapy treatments.

3.4. Recruitment and enrolment

Following ethics approval from the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (HREC: 423/2013), active recruitment took place in the GSH Department of Radiation Oncology. The patients who presented for their follow-up appointment were approached by the researchers to ask if they were experiencing any problems after breast cancer treatment. Probing and selective questions (Table 2) were used to screen whether the patient was experiencing the problems that might indicate AWS. The primary diagnostic criterion was a web of axillary skin with a palpable cord(s) that tensed up with abduction of the shoulder and extended along the ipsilateral arm towards the thumb. The cord or web could be accompanied by secondary symptoms of decreased ROM of the upper limb and pain in the arm and around the area of surgery.

Table 3.2*. A list of questions used to identify potential patients with AWS.*

Sample probing questions asked of patients during recruitment		
Do you speak Afrikaans or English?	YES	NO
Are you here for a breast cancer check-up?	YES	NO
Have you received surgery for breast cancer?	YES	NO
Are you having any problems that came about after the treatments?	YES	NO
Are you feeling any pain in the shoulder and/or armpit?	YES	NO
Are you having problems in moving your shoulder on the treated side?	YES	NO
Do you feel any pulling in the armpit?	YES	NO
Do you feel a cord or tight structure when lifting your arm?	YES	NO

If the patient was identified as experiencing the clinical symptoms of reduced ROM, pain and axillary tightness, a clinical exam was carried out by the supervisor in a private room for inspection of the axilla for the presence of cording. After positive identification, the researcher would sit down with the patient to go through the study information leaflet (see Appendix B) and, if the patient was interested in participating, the researcher would ask the patient to fill out their contact details and name on a reply slip (see Appendix B) so she could be contacted for the first appointment of the study.

Due to the difficulty of recruiting patients via the manner described above, patients that presented with AWS during recruitment for a second study by the supervisor were also approached for participation after presenting with the required symptoms during a questionnaire.

During the patient sampling stage (Diagram 3.1), the researcher identified 156 potential patients that were screened for AWS. Of the potential patients, 35 patients were experiencing the symptoms indicative of the syndrome of which only 21 patients actually presented with one or multiple axillary cords. The patients with the cording were then approached for further participation, of which only eleven patients were willing or able to enter the study.

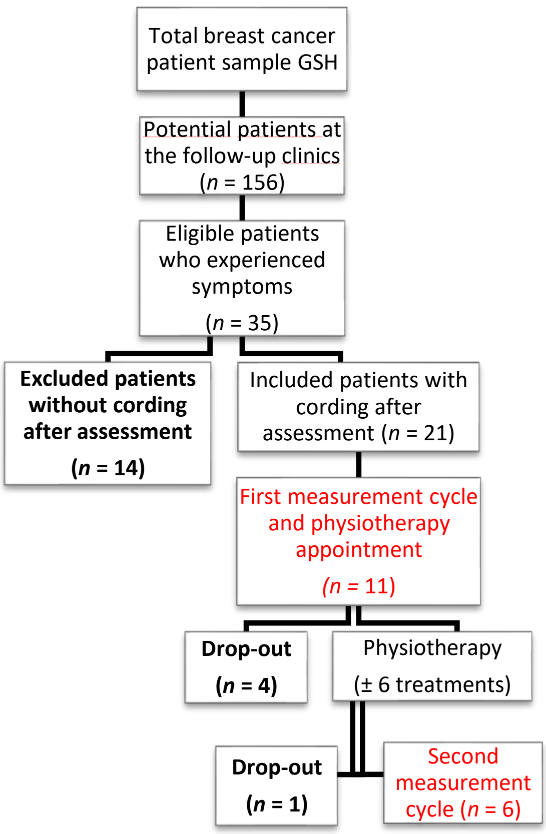


Diagram 3.1. *Patient sampling procedure.*

After the first US appointment, four patients dropped out due to socioeconomic pressures (one), cord resolution before the physiotherapy appointment (two) and one who did not respond to phone calls for physiotherapy. Seven out of eleven patients received up to six physiotherapy treatments after which six took part in the second measurement cycle. One patient was too ill to continue with her physiotherapy treatment and had to withdraw. After recruitment the drop-out rate of the study was five patients.

3.5. Research procedure

3.5.1. Patient consent and first measurement cycle

At the first appointment in the Ultrasound Unit (C10) of GSH, the participant was informed about the aims and objectives of the study. A full explanation of the study procedure, the risks and the benefits of participation were given to the patient at the first appointment. Patients were given the opportunity to discuss anything that was unclear. The participant was also notified that any transport fees to commute to the research locations would be reimbursed.

When the patient had read the consent form for the study (see Appendix B), which was drawn up in accordance to the *Standard Operating Procedures* provided by the UCT Faculty of Health Sciences Human Ethics Committee, she was asked to sign the consent form that was co-signed by a member of the research team for proof of acceptance. By giving consent, the patient agreed to participate in the study and allowed the researchers permission to obtain clinical and demographic information from her healthcare professionals and the hospital files (see Appendix E).

Once the patient consented, data collection occurred in the following measurement sequence. First, the SPADI (Shoulder Pain and Disability Index) questionnaire and the FACT-B (Functional Assessment of Cancer Treatment-Breast) questionnaire to measure quality of life were filled out. After the questionnaires, ROM (range of movement) of both her shoulders was measured and the cord was photographed, documented and measured (see Appendix C+D; Collection Sheet A (i) and (ii)). Lastly, the participant underwent US scans on both affected and unaffected sides. The data collection measures are detailed below.

3.5.2. Patient physiotherapy treatment

After the first measurement cycle, the patient underwent treatment by a physiotherapist on the team. The treatment focus and goals were determined by the standard norm of the therapist for the treatment of AWS. An impairment-based treatment approach (Fourie & Robb, 2009) was used to address the personal needs of the patients but set within limits to maintain standardisation across all participants.

The literature suggested that approximately six to thirteen treatments of 30 minutes each spread over one to two months was sufficient for resolution of all the symptoms of AWS (Josenhans, 2007; Moreau *et al*. 2010; Fourie & Robb 2009). The number of treatments for each individual patient was established by the physiotherapist depending on the severity of the symptoms, but a limit of no more than six treatments was given due to time constraints of the study. Each treatment session lasted about an hour and a homework programme was issued to all patients tailored to their specific needs. The physiotherapist assessed patients independently and prescribed treatment accordingly. The specifics of each treatment and the patient symptomology and improvements were documented by the physiotherapist (see Appendix F and G; Data Collection Sheet C and physiotherapist notes).

3.5.3. Second measurement cycle

When the physiotherapist had decided on the last physiotherapy session (treatment six or fewer, depending on how much improvement could still be made), the participant was asked to return within a week of her last appointment for a second measurement cycle. The second cycle entailed the same procedure as the first measurement cycle.

3.5.4. Patient-reported outcome measures and data collection methods

3.5.4.1. Shoulder pain and disability index (SPADI)

The SPADI is a reliable and sensitive patient reported outcome measure of patients' experience of pain and disability (Williams, Holleman & Simel, 1995). The questionnaire gives independent scores for pain and disability which were used for data analysis. The questionnaire contains two domains: pain and disability. The pain domain contains five items and the disability domain contains eight items. All of the items are questions relating to how much pain and how much disability the patient experiences. The items are answered by using a scale from 0-10 with 0 indicating "no pain" and 10 "the worst pain imaginable". For each domain the scores are made up of the addition of all individuals item scores giving a maximum score of 130 for the whole questionnaire. A total SPADI score is given as a percentage of the maximum score. The higher the score the more disability and pain the patient experiences. The patient filled in the questionnaire by herself but, in case anything was unclear, the researcher would assist in answering the questions, avoiding any bias in their answering.

3.5.4.2. Functional assessment of cancer treatment – breast (FACT-B)

The FACT-B is a well-validated, multi-dimensional patient self-report questionnaire which measures physical, social, emotional and functional well-being and additional breast cancer concerns in separate subscales (Fallowfield *et al*., 1999). Its psychometric properties show high reliability and internal consistency and is simple and quick to fill out (Fallowfield *et al*., 1999). The patient filled in the FACT-B questionnaire by herself after the SPADI. If she needed any clarification, the researcher would help but made sure to avoid any bias. The questionnaire is divided into five sections: Physical, Social, Emotional, Functional and Additional, with questions in each around those themes. Each question is worth 4 marks with a total score of 140. The higher the score, the better the quality of life measure.

3.5.4.3. Shoulder range of movement (ROM)

Active shoulder ROM of the patient was measured using a standard goniometer, which has high inter-observer reliability (Johansson *et al*., 2001). Only active movements were measured as they were considered to be the best representation of the patients' dysfunction and debilitation. The patient was asked to stand with her back towards a wall so that bony landmark points at which the goniometer would be positioned could be marked on the patient with a washable pen (Figure 3.1). The patient was then asked to abduct and forward flex her arm. After that she was asked to move with her face towards the wall and extend her arms as far as possible within her levels of pain and discomfort. Lastly, the patient was asked to lie on her stomach on the plinth for measurements of internal and external rotation.

Figure 3.1. *Locating the bony landmark and marking it with a ballpoint pen.*
Permission was obtained from the model.

For **abduction**, the goniometer axis was placed at the anterior aspect of the glenohumeral joint, 1.3 cm inferior and lateral to the coracoid process. The stationary arm was held parallel to the sternum and the moveable arm parallel to the longitudinal access of the humerus (Clarkson & Gilewich, 1989) (Figure 3.2).

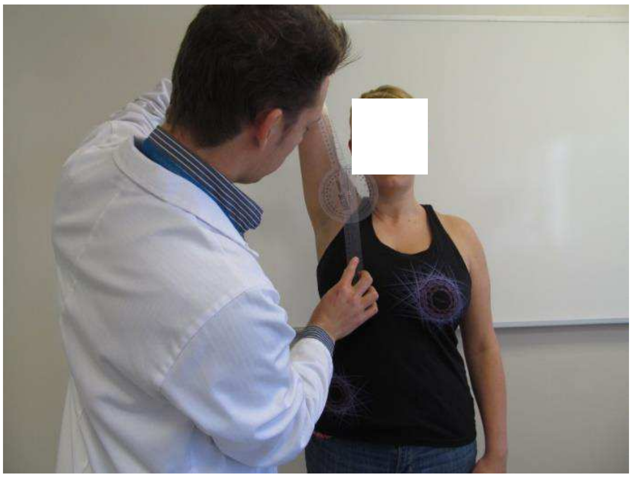


Figure 3.2. *Goniometric measurement of abduction. Permission was obtained from the model.*

For **forward flexion and extension**, the goniometer was placed at the lateral aspect of the centre of the humeral head, 2.5 cm inferior to the lateral aspect of the acromion process. The stationary arm of the device was held parallel to the lateral midline of the trunk, whereas the moveable arm was pointing towards the lateral epicondyle of the humerus (Clarkson & Gilewich, 1989) (Figure 3.3).

Figure 3.3. *Goniometric measurement of extension (left) and forward flexion (right). Permission was obtained from the model.*

For **internal and external rotation**, the patient was asked to lie in prone position on the plinth with her elbow in a 90° angle. The bony point of interest was marked and the patient was asked to move the lower arm as far back as she could for internal rotation of the shoulder and forward for external rotation. Measurements were taken at the highest and furthest points the patient could move within pain and discomfort levels. For internal and external rotation, the goniometer axis was placed on the olecranon process of the ulna, with the stationary arm perpendicular to the floor and the moveable arm to the longitudinal axis of the ulna towards the ulnar styloid process (Clarkson & Gilewich, 1989) (Figure 3.4).

Figure 3.4. *Goniometric measurement of external (left) and internal (right) rotation. Permission was obtained from the model.*

3.5.4.4. Cord length

Whilst lying on the plinth in supine position, the participant was asked to abduct and externally rotate her arm to her maximum within levels of pain and discomfort, which would allow for full exposure of the cord. The length of the cord was then determined using digital callipers from the points of visual and palpable tethering (Figure 3.5). Cord length was measured with a measuring tape in a previous study (Leduc *et al*., 2009). There is, however, little information on the validity and reliability of using the measuring tape method. Digital callipers are widely used in other clinical measurements due to it being a valid and reliable measurement tool (Ebaugh, Spinelli & Schmitz, 2011); therefore, it was chosen as the measurement tool of choice. To make sure the measurement was accurate, the researcher always verified the points of tethering with the research assistant. In addition, photographic record of the cord was taken (excluding the patient's face for anonymity). If more than one cord was visible, the thickest and clearest ones were documented.

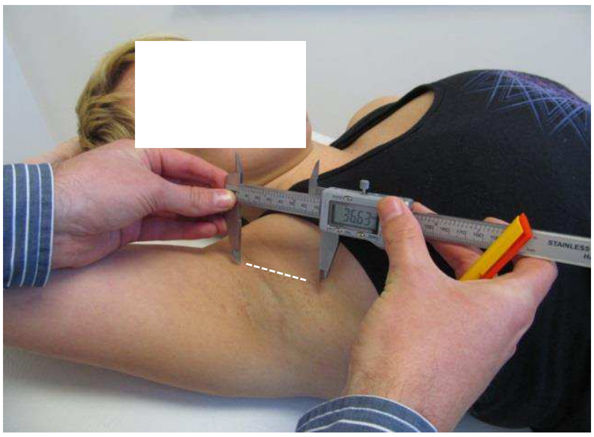


Figure 3.5. *Measurement of a hypothetical cord (dotted line) with a digital calliper. Permission was obtained from the model.*

3.5.4.5. Ultrasonography (US)

3.5.4.5.1. Machine details and location

The present study utilised a Toshiba Xario™ Diagnostic Ultrasound System (Model SSA 660A) with a Toshiba Linear Array transducer (Model PLT 120-4BT; 12 MHz frequency). Located in the Ultrasonography and X-Ray Department of Radiology, Groote Schuur Hospital, the new and recently calibrated machine is used for clinics during the day and access was granted for use after hours in the present study. It was the most modern machine available and had the highest frequency probe available (12 MHz) to allow for the increased detail needed in the scans. For all the scans the ultrasound system was put in a pre-programmed musculoskeletal setting (MSK) with a frequency of 12 MHz and a penetration depth of 5 cm. Advice on the workings of the machine were given by the personnel in the unit.

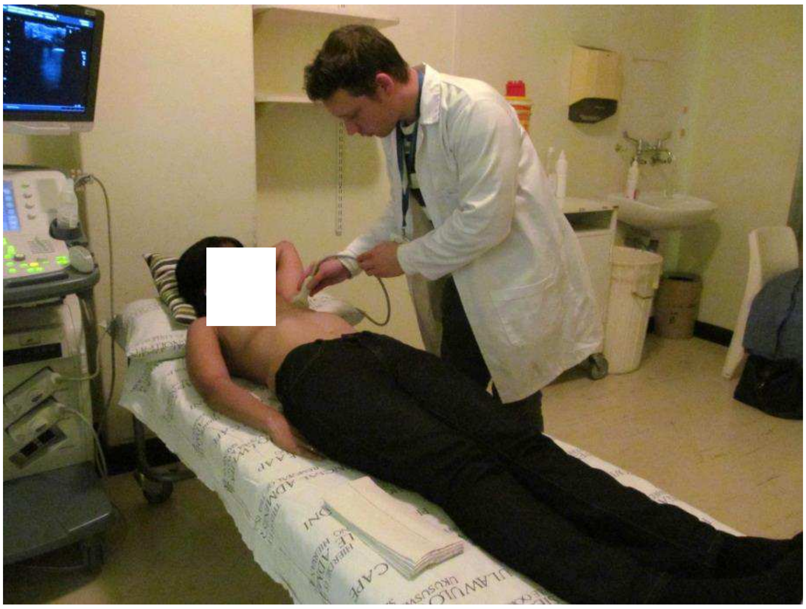


Figure 3.6. *Ultrasound procedure with the patient in the ABER position. Permission was obtained from the model.*

3.5.4.5.2. Procedure

The patient was asked to undress to her bra and asked to lie down in the supine position on the plinth. For full disclosure of the cord, the patient was asked to hold her arm in abduction-external rotation with her hand behind her neck but within patient level of pain and discomfort.

The US procedure always commenced on the right arm with the same researcher doing the scanning. Gel was applied to the probe after which it was placed on the most inferior point of tethering of the cord in the axilla in longitudinal orientation, in line with the main cord. The cord was followed systematically externally starting from the inferior point of tethering moving to the most visible point of tethering superiorly. In the case of multiple cords, only the most obvious one was followed to minimise the time and discomfort for the patient. The transducer was held directly superior to it and was placed lightly onto the skin to avoid much indentation on the scans (Figure 3.6). After agreement was reached between the researcher and the researcher's assistant on the best and most clear scans, the assistant pressed the button to save the scan.

To show the fascia continuity below the cord, static snapshots were taken during real-time dynamic scans of the cord following its trajectory moving from one probe head-width superior and inferior to the cord in longitudinal probe positions, and were aligned to show wider fascial continuity. At the midway point of the cord, one transverse scan was taken to show a cross-sectional view. Furthermore, a video of the arm in movement (neutral – abduction-external rotation) was taken at the midpoint of the cord in longitudinal probe position to highlight the tension on the fasciae and fascial gliding (Diagram 3.2).

The described procedure was replicated on the unaffected side or, in the case of a double mastectomy, on both sides for comparative purposes.

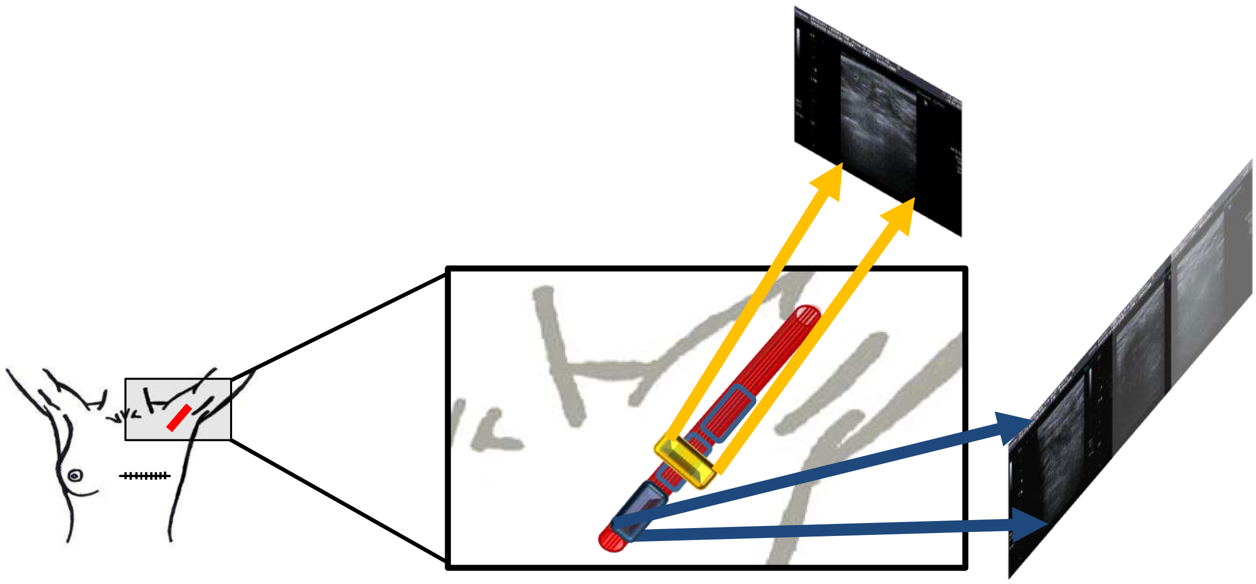


Diagram 3.2. *Diagram detailing the ultrasonography procedure. The inset highlights the cord and the positioning of the ultrasound probe (as depicted by the rectangles) to obtain a longitudinal (blue) and cross-sectional/transverse (yellow) view of the cord on the ultrasonographs. The longitudinal graphs were obtained along the midline of the full visible cord whereas the transverse ultrasound was obtained at the midpoint of the structure. The longitudinal ultrasounds were consecutively aligned to show a more continuous view of the cord structures and wider fascial involvement. Image adapted from* [*http://www.msdlatinamerica.com*](http://www.msdlatinamerica.com)*.*

3.5.4.6. Photographs

Detailed photographs were taken of the patients' cords. Depending on where the cords reached, the photographs depict the axilla, arm, forearm and chest of the patient. The patient's face was never photographed, or her face was concealed, for anonymity reasons. The pictures were taken using a standard Canon PC1677 Digital Camera in auto-mode.

3.5.4.7. Magnetic resonance imaging (MRI)

For the exploration of alternative imaging methods to improve our knowledge of the anatomical structures in and surrounding the cord, MRI was chosen. After additional ethics clearance was obtained (HREC: 098/2014), only a single patient was chosen to participate because of the expense of the method. Due to the discomfort of lying still within the MRI machine for an extended period of time, the patient would need to be able to hold her arm in the ABER position for which Patient FS/2013/11 qualified. The patient was imaged using a Philips Ingenia 3.0T MRI machine and was scanned in long axis STIR PDFS T1, as well as short axis STIR T1 to get a dual view as well as a better indication of the tissues present in and around the cord (Figure 3.7).

Figure 3.7. *MRI set-up with patient in the ABER position. Permission was obtained from the model.*

3.5.5. Patient folder information

Clinical and demographic details of the patients were collected from the General Hospital and Radiology patient folders at Groote Schuur Hospital. The supervisors assisted in obtaining the chosen information and included diagnosis (type of breast cancer, tumour variables), treatment information (type: surgery, adjuvant therapies; side, area, frequency and history) and physiotherapy information (treatments, dates, frequency). For a full list of items, refer to Appendix E; Data Collection Sheet B.

3.6. Data analysis

3.6.1. Numerical data

Numerical data from all the measurements were analysed using the programme STATISTICA 12 (StatSoft®, 2013). Normality was assessed using the Shapiro-Wilk test. As the sample was not normally distributed, non-parametric Kruskal-Wallis and Spearman rank tests were done to observe any significant differences and relationships between the data before and after physiotherapy and between arms. The statistical data were used to establish possible trends in the data, and supporting established trends, not for generalising to a larger cohort due to the limitations of the study.

Due to the small and non-normal sample, medians were used as the non-parametric equivalent of average and percentage change, and differences were used to observe how much patients improved after physiotherapy and how much the affected arm differed from the unaffected arm. Furthermore, percentage contribution to total score in the SPADI and FACT-B questionnaire were used to establish which item contributed most to the overall score as an indicator of which specific behaviour most affected patients pre- and post-physiotherapy.

A Bonferroni correction controlled for inflated familywise error associated with multiple pairwise comparisons and are reported in the appropriate sections of the results.

3.6.2. Categorical data

The categorical data that arose from the clinical patient records was attributed a number and was analysed with the numerical data as described above. Categorical variables were submitted to chi-squared testing to assess whether the variables are associated with differences between and within patients in the larger GSH cohort.

3.6.3. Qualitative data

Being the main focus of the study, data from the description and explanation of the fascial continuity, fascial and cord changes and fibrotic development were compared within and between the participants, before and after physiotherapy treatment. Furthermore, trends that were visible within the numerical data were discussed with the qualitative and physiotherapy data in mind.

3.6.3.1. US analysis

Static US analysis was done by means of a summary table as shown in Leduc *et al*. (2014) to identify which patients showed which features on the US scans (see Appendix H). The current study used descriptors that were described in the fascia and AWS literature (Stecco, 2015; Langevin *et al*., 2011; Leduc *et al*., 2014; Koehler, 2013) (Table 3.3). Dynamic ultrasound analysis was done comparing the tissue glide and movement between unaffected and affected arms, before and after physiotherapy. The videos can be accessed via https://drive.google.com/open?id=1-o4EHuPy-IcsQBk1X-fVroPXviPruJlg

3.6.3.2. MRI analysis

MRI analysis was provided by the radiologist at the site of the scan and was rewritten in line with the descriptor definitions used in US analysis.

3.6.3.3. Descriptor definitions

Standardised definitions to describe the features on US and MRI were used to prevent confusion due to the different interpretations of the same terms used in the literature (Table 3.3). The definitions were adapted from the literature (Stecco, 2015; Langevin *et al.*, 2011; Leduc *et al.*, 2014; Koehler, 2013).

Table 3.3. *The definitions used to describe features on the ultrasound and MRI scans.*

Descriptor definitions
Adhesions: vertical connections between parallel planes
Densification: impaired gliding potential between layers
Echogenicity: the intensity of the signal on ultrasound; hyper=increased, hypo=decreased
***Echotexture**: an overall appearance of speckles, haziness; can be either smooth (homogenous) or coarse (heterogenous)
Fascial continuity: no disruption in the fascial planes, continuous lines
Fibrosis: thickening of the individual fascial layers and/or increased echogenicity
Heterogeneity: a varied overall appearance
Homogeneity: a similar overall appearance
Honeycomb structure: resembling a hexagonal structure
Reduced gliding potential: reduced gliding on dynamic ultrasound videos
Superficial fascia: the multiple echogenous layers on ultrasound in the hypodermis

* The term was borrowed from the ultrasound terminology describing fibrosis in liver and lungs (Perez *et al.* 2007).

3.7. Data safety and monitoring

All the information that was gathered during the data collection appointments was noted on Data Collection Sheet A which was divided into two parts for the two separate appointments (see Appendix C + D). The data which were obtained from the medical records and the health professionals were compiled on Data Collection Sheet B (see Appendix E). Physiotherapy-related data were compiled on Data Collection Sheet C (see Appendix F). Whenever new data were acquired, they were saved electronically on the computer the same day after which the physical copy was securely stored in the supervisor's research office. Back-ups were stored on a separate hard drive which was stored safely and separately from the physical data.

The study ran according to the *Protection of Personal Information Bill* (2009). All the data obtained in the study was coded with study numbers (FS/2013/participant#), on both the computer and on physical copies. The master key was kept in a secure location (the supervisor's research office) and held separate from the data to maintain anonymity and protection of privacy. Only the principal investigator and the postgraduate student involved knew the location and had access to it.

3.8. Research procedure limitations

US is an operator-dependent modality. Because of the patients' inability to maintain the same position for an extended period of time, measurements and scans could not be repeated to establish reliability. The current study attempted to ensure the reliability of the findings by including the following:

1. The anatomical location of each patient's cord in the axilla was provided as the cord positions differed per person, which indicated the location where US scans were taken.
2. US scans were analysed using anatomical atlases (Standring, 2008; Stecco, 2015) to determine more accurately the anatomical structures at the cord's location and guided by the anatomical knowledge of the supervisors.
3. A description of the US settings and analysis method was given.
4. The same observer carried out all US scans and other measurements. The researcher that conducted the scanning has experience using US, was adequately trained and was supervised by a senior staff member when necessary.
5. There were always at least two researchers present: one of the team and an assistant who was familiarised with the protocol. A consensus between the two researchers during the measurement cycle was reached to obtain the best representation of the area of interest on US and the most correct measurements. In case of illness, another team member (who had been updated about previous sessions and was able to replicate the procedures) would take over.
6. For full transparency, most of the data including US scans are provided and US videos may be downloaded for future analysis.

Chapter 4: Results

4.1. Introduction

The results chapter is set out in accordance with the aims and objectives described in Chapter 1 and describes the general findings and trends of the study. The sections include patient demographics and clinical data, statistical analyses, patient outcome measure exploration and summaries of imaging findings in relation to outcome measures. Detailed case analyses can be found in Chapter 7 – Supplementary Information.

4.2. Patient demographic and cancer profile

A summary of the patient demographics and clinical cancer data of the study sample is listed in Table 4.1. Of the study sample (n = 11), 81% was over 40 years of age and 27% was over the age of 60 years. Two patients received bilateral mastectomies. One received a sentinel lymph node biopsy, whereas all patients had axillary clearances. Over 90% of individuals had more than six nodes removed, with 58.3% of the sample having between 0-5 positive nodes. The most common tumour size was found within the 20-39 mm range (36.6%).

Two patients received radiation therapy before surgery and seven after surgery, with one person receiving two doses after surgery. Five patients received chemotherapy pre-surgical treatment and eight post-surgical treatment, whereas two patients received hormonal treatment before surgery and seven after surgery.

4.3. Patient AWS symptomology and study outcome measures

Table 4.2 shows that there is a very wide range of number of days from surgery to the first measurement time with patients presenting with AWS from 57 to 1 455 days (± four years) after surgery. Six out of eleven patients presented more than a year with cording before physiotherapy. Three out of six patients continued to have a cord after physiotherapy of which two had surgery more than a year ago.

Nine out of eleven patients who participated in the study self-reported pain over the shoulder or axilla and eight reported limited movement of the upper limb. After physiotherapy, the fraction decreased to one out of six who continued to have pain and three still had a remainder of the cord present, but it was much reduced.

Table 4.1. Summary of patient demographics and clinical data.

Demographics and cancer profile

Characteristic	Patient %	Patient Frequency
Age		
<40	18.2	2
40-49	27.3	3
50-59	27.3	3
>59	27.3	3
Breast surgery		
Single mastectomy	81.8	9
Double mastectomy	18.2	2
*Axillary surgery**		
SLND (<4 nodes)	9.1	1**
ANC	90.9	11#
*Number of resected nodes**		
<5	8.3	1
6-15	58.3	7##
16-25	33.3	4##
*Number of positive nodes**		
0-5	58.3	7
10-15	42.7	5#
Tumour size		
<19	18.2	2
20-39	36.3	4
40-59	9.1	1
60-79	18.2	2
>80	18.2	2#
Histological type		
Invasive ductal	81.8	9
Lobular	18.2	2
Stage		
II	18.2	2
III	45.5	5
IV	36.3	4
*Grade^*		
I	9.1	1
II	45.5	5
III	36.3	4
Lymphovascular invasion	36.3	4
Multifocality	54.5	6
Receptorial status		
PR-positive	27.3	3
ER-positive	72.7	8
HER-2-positive	54.5	6

Characteristic	Patient %	Patient Frequency
Neoadjuvant treatments		
Radiation therapy		
1 course	9.1	1
2 courses	9.1	1
Chemotherapy		
1 course	36.3	4
2 courses	9.1	1
Hormonal therapy		
2 courses	9.1	1
3 courses	9.1	1
Adjuvant treatments		
Radiation therapy		
1 course	54.5	6
2 courses	9.1	1
Chemotherapy		
1 course	45.5	5
2 courses	27.3	3
Hormonal therapy		
1 course	36.3	4
2 courses	27.3	3

* The number of patients in the category add up to more than 11 as one patient had a lymph node resection bilaterally

** The individual received SLND on only one side but had a bilateral mastectomy

The category examined the same individual twice for each side that treatment was received

The categories contained the same individual but for which each side differed

^ For one individual no tumour grading could be extracted from the patient folder

/ The category contained patients who received the same type of neoadjuvant treatment as adjuvant treatment

The other three patients experienced full relief of all symptoms. Nine out of eleven patients had one cord, whereas two patients had a true axillary web with two dominant cords. Just less than half of patients (46.2%) showed a cord of between 90-109 mm with two patients presenting with a longer cord. After physiotherapy, the cord resolved in 50% of the sample with only one patient still presenting with a cord that was over 89 mm, one between 70-89 mm and one with a cord that was between 50-69 mm in length.

Table 4.2. *Symptomology of patients in percentages and number of patients per category.*

Signs and symptoms		
	Patient	
Characteristic	**%**	**Frequency**
*Time from surgery to Observation Point 1**		
< 3 months	18.1	2
3 months – 1 year	23.0	3
> 1 year	54.5	6
Time from surgery to Observation Point 2		
3 months – 1 year	33.3	2
> 1 year	66.7	4
*Symptomology present before physiotherapy***		
Pain present	81.8	9
Reduced ROM present	72.7	8
Cording present	100	11
*Symptomology present after physiotherapy***		
Pain present	14.2	1
Cording present	42.9	3
Full resolution of symptoms	42.9	3
Cord side		
Left	36.3	4
Right	45.3	5
Bilateral	18.1	2
Number of cords		
1	81.9	9
2	18.1	2
Cord length before physiotherapy (mm)		
50-69	15.4	2
70-89	23.0	3
90-109	46.2	6
>110	15.4	2
Cord length after physiotherapy (mm)		
50-69	33.3	1
70-89	33.3	1
90-109	33.3	1

* Median time was 368 days (min. 57 – max. 1455 days)
** Patient-reported

4.4. Statistical analysis of the numerical data

4.4.1. Normality testing

A Shapiro-Wilks test was performed to evaluate the normality of the study data distribution. The test showed that the majority of the variables were not normally distributed. Normalisation of the data was attempted by log or square-root transformations which did not yield normal data, and hence non-parametric tests were used in the subsequent report.

4.4.2. Spearman rank correlations

Spearman rank correlation tests were performed to assess the relationship between cord length, ROM measures, time from surgery until Observation Point 1, FACT-B Functional and Physical domain scores and total score, SPADI total and domain scores, age, and number of resected nodes before and after on the affected side (Association Matrix 4.1) and unaffected side (Association Matrix 4.2).

In the affected arm, at the Bonferroni-corrected level of significance, before physiotherapy there was a significant positive association between cord length and internal rotation (r = 0.791). After physiotherapy, there was a significant negative association between cord length and SPADI Pain (r = -0.895). The number of resected nodes was significantly positively associated with age (r = 0.847).

In the unaffected arm there was a significant negative association of flexion with age (r = -0.900) after physiotherapy, but no significant associations before physiotherapy.

Association matrix 4.1. *The Spearman rank associations for outcome measures of cord length, ROM, time from surgery to the first observation point (Surg-Obs 1), FACT-B, SPADI, age and number of resected nodes (number of nodes) for the affected side. The darker red part of the matrix indicates <u>before</u> physiotherapy, the lighter part <u>after</u> physiotherapy. The numbers in red are significant associations, while the numbers in blue are significant associations after the Bonferroni correction (p < 0.001).*

VARIABLE	Cord length	Abduction	Extension	Flexion	External rotation	Internal rotation	Surg-Obs 1	Total Physical	Total Functional	Total Fact-B	SPADI Pain	SPADI Disability	Total SPADI	Age	No. of nodes
Cord length		0.348	-0.050	**0.633**	0.152	**0.791**	-0.444	-0.069	0.033	-0.041	-0.221	-0.240	-0.223	-0.494	-0.419
Abduction	-0.434						-0.219	0.025	-0.073	-0.263	-0.295	-0.330	-0.271	-0.224	0.033
Extension	**-0.783**						**0.626**	0.379	0.289	0.311	-0.151	0.057	0.044	0.094	0.156
Flexion	-0.149						-0.145	0.213	0.172	-0.007	-0.528	-0.447	-0.517	-0.510	-0.215
External rotation	-0.729						-0.140	-0.117	-0.159	-0.352	0.072	-0.180	-0.094	-0.424	-0.395
Internal rotation	-0.236						-0.269	-0.108	-0.024	-0.029	-0.035	-0.130	-0.062	-0.298	-0.373
Surg-Obs 1	0.497	-0.739	-0.028	-0.346	-0.090	0.018		**0.755**	**0.598**	0.492	-0.358	-0.257	-0.286	0.358	0.203
Total Physical	0.266	-0.111	0.113	-0.019	-0.371	-0.741	0.411							0.348	0.304
Total Functional	0.164	-0.259	0.396	0.019	0.000	-0.259	0.748							0.311	0.490
Total FACT-B	-0.060	0.018	0.358	0.036	-0.090	-0.739	0.236							0.400	**0.634**
SPADI Pain	**-0.895**	0.306	0.688	0.300	0.721	0.360	-0.346							-0.059	-0.366
SPADI Disability	0.079	-0.679	-0.436	-0.739	-0.393	-0.143	0.126							-0.164	-0.087
Total SPADI	-0.378	-0.324	-0.138	-0.482	-0.036	-0.180	-0.282							-0.155	-0.177
Age	-0.020	-0.306	0.413	-0.164	0.054	0.342	0.673	0.262	0.673	0.164	0.073	0.090	-0.209		0.256
No. of nodes	0.039	-0.536	0.327	-0.505	-0.071	-0.143	0.739	0.556	**0.778**	0.487	-0.072	0.286	0.000	**0.847**	

Association matrix 4.2. *The Spearman rank associations for outcome measures of ROM, time from surgery to the first Observation Point (Surg-Obs 1) and age for the unaffected side. The darker blue part of the matrix indicates <u>before</u> physiotherapy, the lighter part <u>after</u> physiotherapy. The number in blue is the significant association after the Bonferroni correction (p < 0.005).*

VARIABLE	Abduction	Extension	Flexion	External rotation	Internal rotation	Surg-Obs 1	Age
Abduction						0.183	-0.293
Extension						0.283	-0.552
Flexion						-0.367	-0.628
External rotation						0.217	0.000
Internal rotation						0.350	-0.351
Surg-Obs 1	-0.500	-0.103	-0.300	0.600	0.300		0.234
Age	-0.100	0.616	**-0.900**	-0.200	0.600	0.400	

4.4.3. Kruskal-Wallis difference testing

Kruskal-Wallis tests were performed to determine statistical differences before and after physiotherapy within the outcome measures of ROM (affected, unaffected), SPADI domain scores, FACT-B scores and cord length.

4.4.3.1. ROM

For the affected side, statistically significant (Bonferroni-corrected p-value < 0.01) results were observed for abduction (p = 0.0078) and flexion (p = 0.0062) , which all showed a significantly higher ROM post-physiotherapy. On the unaffected side, no statistically significant differences were observed between affected and unaffected ROMs before or after physiotherapy.

4.4.3.2. SPADI, FACT-B and cord length

There was a statistically significant reduction noted for SPADI Pain (p = 0.0003), SPADI Disability (p = 0.0055) and SPADI Total (p = 0.0008) after physiotherapy (Table 4.3). No significant differences were observed for cord length or FACT-B scores.

Table 4.3. *A summary of the descriptive statistics (median, min and max) and p-values of Kruskal-Wallis tests done on cord length, SPADI domain scores and FACT-B domain scores before (B) versus after (A) for the affected side. The number in red shows significant differences. The numbers in blue are significant differences after the Bonferroni correction (p < 0.007).*

Outcome measure	Median	*p*-value B vs A
SPADI Pain before	33.00	
SPADI Pain after	6.00	**0.0003**
SPADI Disability before	39.00	
SPADI Disability after	10.00	**0.0055**
Total SPADI before	71.00	
Total SPADI after	20.00	**0.0008**
FACT-B Physical total before	16.00	
FACT-B Physical total after	14.50	**0.8424**
FACT-B Functional total before	21.00	
FACT-B Functional total after	23.50	**0.5727**
Total FACT-B score before	95.00	
Total FACT-B score after	102.17	**0.6626**
Cord length before	92.64	
Cord length after	79.04	**0.0097**

4.4.4. Cohort results for SPADI and FACT-B

A chi-squared test was performed to observe whether baseline data for the current study sample was representative of the larger GSH breast cancer treated patient cohort. The before (n = 13) and after data (n = 7) of FACT-B and SPADI answers for individual items were compared to the cohort consisting of three other study samples taken in previous years (Shamley et al., 2012-2014 [unpublished raw data]) (n = 119). The test showed no significant difference between the scores and groups (p > 0.057) with the exception of SPADI item 'lying on the involved side' (p = 0.003), SPADI item 'reaching high' (p = 0.036) and the FACT-B item 'I am close to my friends' (p = 0.020) before physiotherapy.

Further analysis showed a higher percentage of patients that scored 7 or higher for SPADI item 'lying on the involved side' (46% of individuals in the current study compared to 28% in the total group) and SPADI item 'reaching high' (77% of individuals in the current study compared to 36% in the total group) in our sample group before physiotherapy compared to the larger patient group or after physiotherapy. Furthermore, there was a higher percentage of patients who scored a 1 or 0 for FACT-B item 'I am close to my friends' for our sample group at baseline before physiotherapy compared to the larger population (36% in the current study compared to 21% in the total group).

Overall, apart from the abovementioned items, there were no statistical differences in the other 46 items (p > 0.057) between the samples of the present study before and after physiotherapy and the larger population sample; thus the current study sample was used here as representative of the larger population group in terms of SPADI and FACT-B responses.

4.5. General ROM, SPADI, FACT-B

4.5.1. Ranges of scores

Table 4.4. *Different ranges of different outcome measures before and after physiotherapy.*

Outcome measure	Range before	Range after
ROM (affected) (°)		
Abduction	65-139	112-171
Extension	24-85	55-66
Flexion	37-132	113-162
Internal Rotation	41-95	50-127
External Rotation	8-92	52-84
SPADI		
Pain (/50)	20-39	0-14
Disability (/80)	8-71	4-22
Total (/130)	22-107	4-26
FACT-B		
Physical (/28)	5-24	9-25
Functional (/28)	13-27	12-27
Total (/140)	80-125	113-162

The scores in Table 4.4 give an overview of the measures of ROM on the affected side, SPADI and FACT-B findings in the patient groups. Comparing the before and after data, and lower and higher limits, the biggest changes appear in ROM (especially abduction and flexion) and SPADI, with FACT-B scores remaining almost the same. Further analysis of the data is presented in the subsequent sections.

4.5.2. ROM change: affected vs unaffected arms

Figures 4.1 and 4.2 show the differences in median percentage change for the affected and unaffected arm after physiotherapy treatment. On the affected arm (Figure 4.1) there was an improvement noted for all movements, with the actions with the highest improvement seen in abduction (48.9%) and flexion (28.3%), followed closely by external rotation (27.4%) and internal rotation (26.3%). Extension was least improved on the affected side with 8% improvement, and showed no change on the unaffected side. However, only the improvements for abduction (p = 0.0078) and flexion (p = 0.0062) reached statistical significance. Similar to the affected side, abduction on the unaffected side showed the most improvement (31.4%) and external rotation improved by 21%. Internal rotation showed a decrease of approximately 8% after physiotherapy on the unaffected arm (Figure 4.2) and flexion showed only a very slight improvement (3%). None of the changes reached statistical significance.

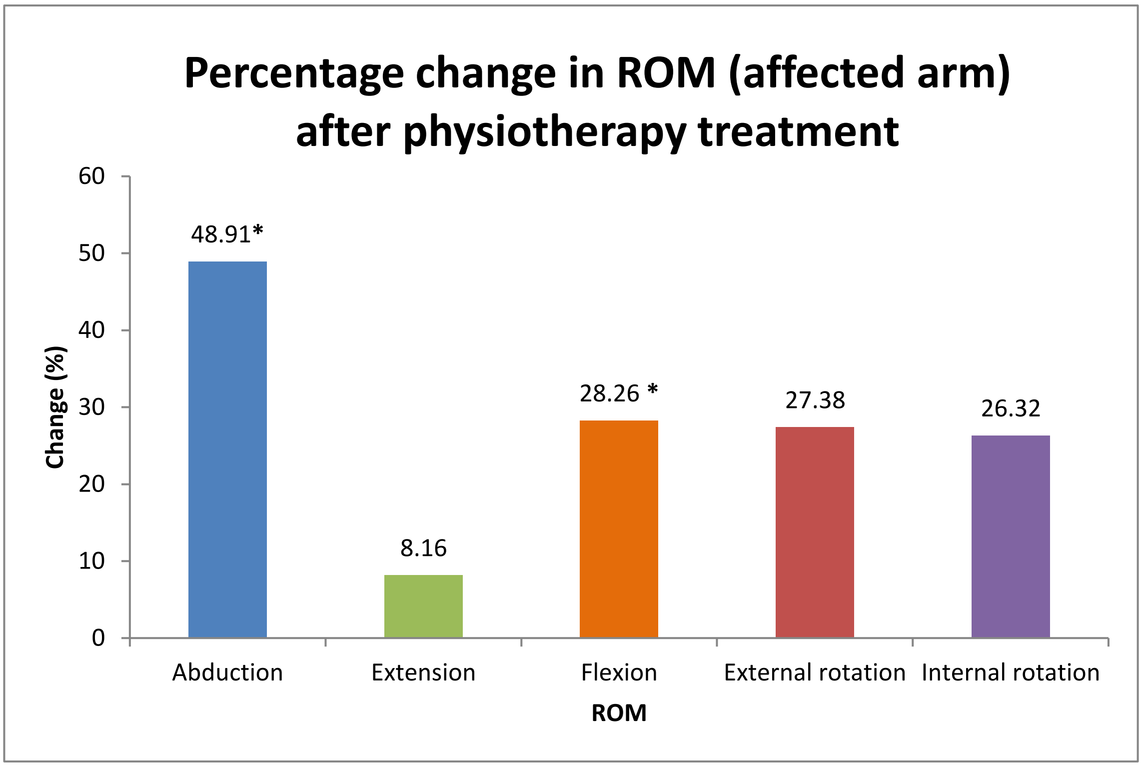


Figure 4.1. *The median improvement of the different movements on the affected arm after physiotherapy. * indicates a significant change of p < 0.01 at the Bonferroni-corrected level of significance.*

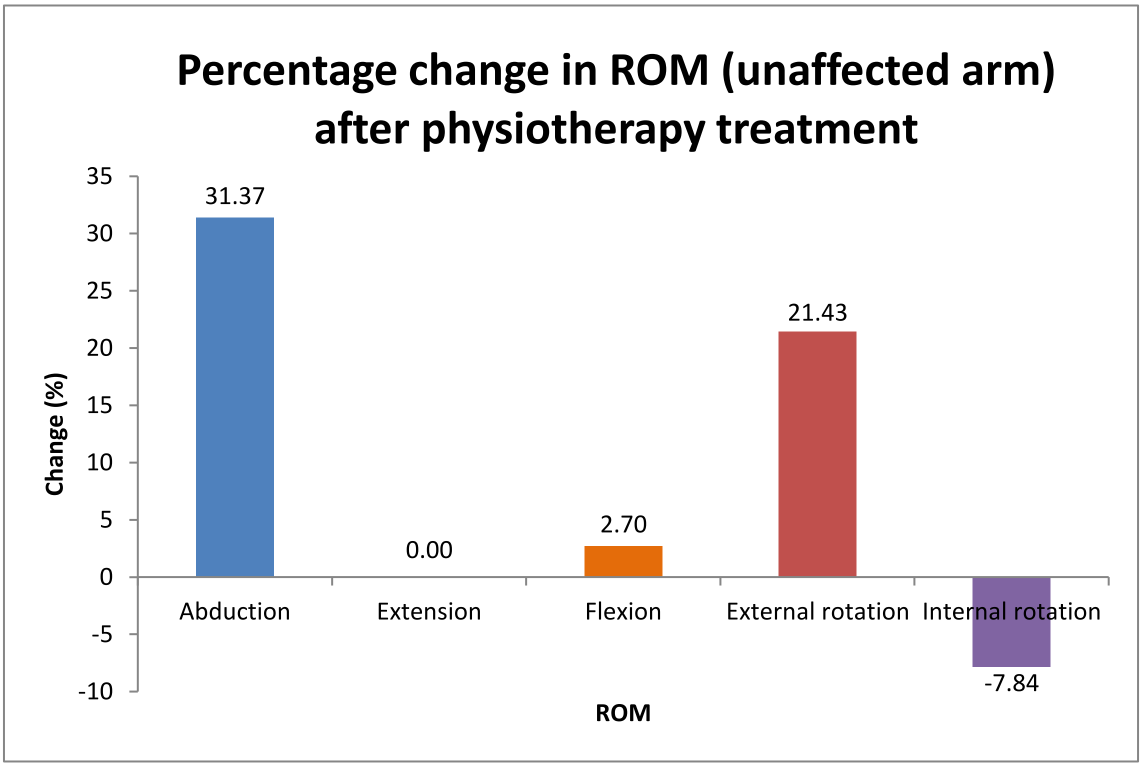


Figure 4.2. *The median change in movement in the unaffected arm after physiotherapy. No statistically significant results were observed.*

4.5.3. SPADI

4.5.3.1. Total SPADI and domain scores

The total median SPADI and component scores are shown in Figure 4.3. The median total SPADI score of 72, which equated to a 55% score is broken down into a 39 = 48.8% disability score and a moderate 33 = 66% pain score. After physiotherapy, the total SPADI score had markedly decreased by 42.7% to 12.3%. The total pain score significantly decreased to 6 = 12% and the disability score significantly decreased to 10 = 13% total disability score.

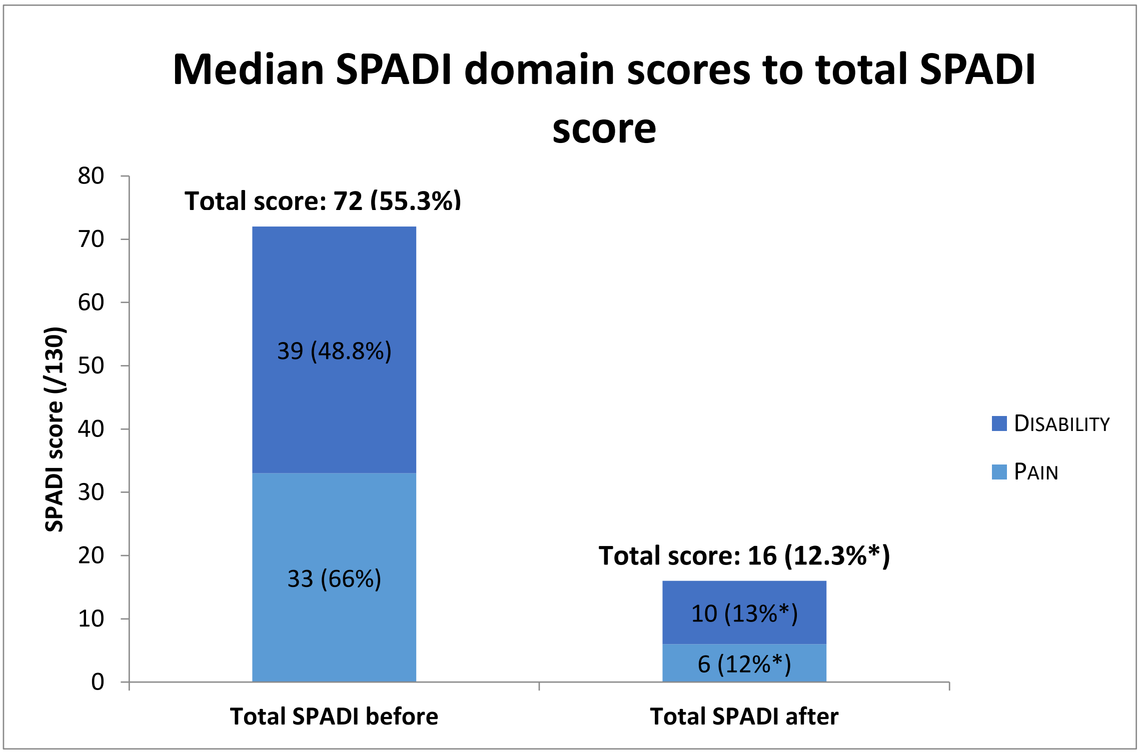


Figure 4.3. *The change in median total SPADI score, before versus after physiotherapy, out of 130. The numbers inside the different subsections refer to the median percentage score for that section, i.e. for pain out of 50 and for disability out of 80. * indicates a significant change of p < 0.007 at the Bonferroni-corrected level of significance (see Table 4.3).*

4.5.3.2. SPADI total score – domain contribution to total score

Figure 4.4 depicts the percentage contribution of the score of each SPADI subcategory to the total median SPADI score before and after physiotherapy. The disability category, which contributes 62% (80/130) to the SPADI score in terms of total score, is shown to contribute only 55% to the total before physiotherapy. The remainder of 45% is thus a higher contribution for pain. The pain category contributes the remainder 38% (50/130) to the total SPADI score and is shown as a slightly lower percentage (36%) after physiotherapy with a little elevated disability contribution of 64%. The distribution difference indicates an improved pain score after physiotherapy.

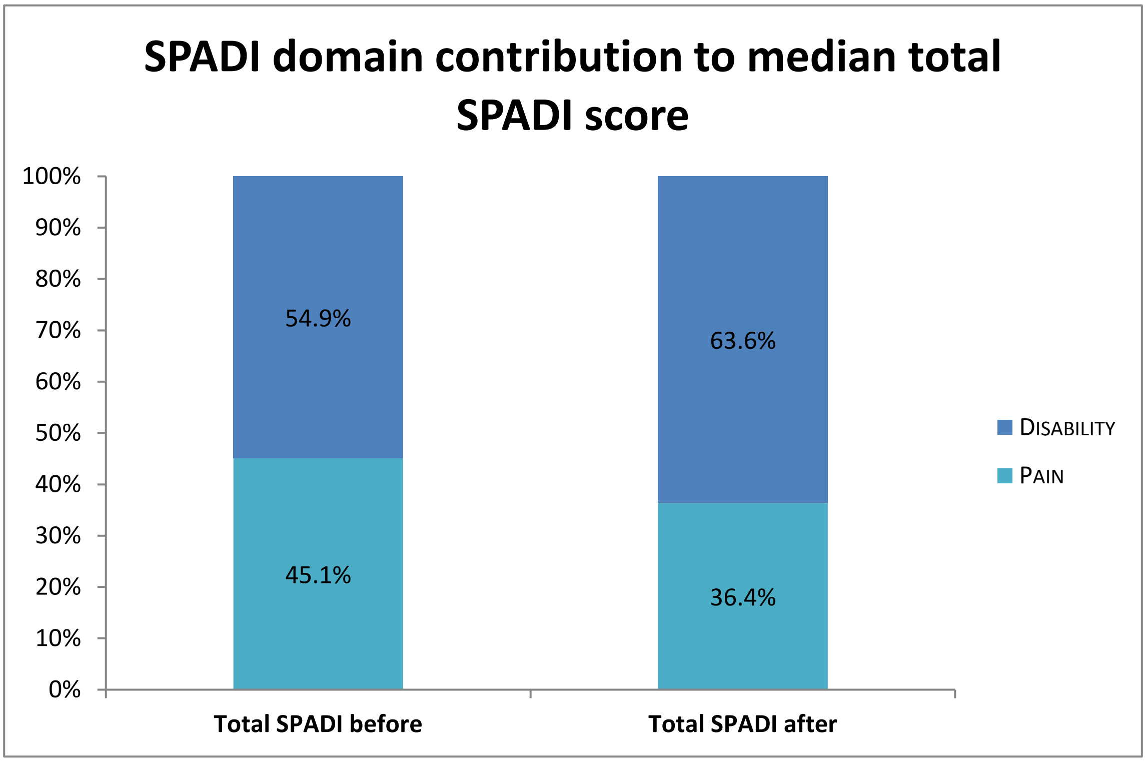


Figure 4.4. *The contribution of the SPADI subcategories to the median total SPADI score before and after physiotherapy.*

4.5.3.3. SPADI pain – item contribution to total score

In Figure 4.5, the differences in contribution of each item to the total median domain score are shown. In the SPADI questionnaire, each item contributed 20% to the overall score. Before physiotherapy, it was observed that the items 'touching the back of the neck' and 'lying on the involved side' contributed most to the score, with the former contributing the greatest (25%). After physiotherapy, the distribution changed with 'at worst' or 'pushing with involved arm' not contributing to the total score, indicating a notable reduction.

4.5.3.4. SPADI disability – item contribution to total score

Figure 4.6 highlights the item contribution distribution for the disability total component of the SPADI. Here the items contributed 12.5% in terms of its items to the total score. Before the physiotherapy treatment it was observed, however, that 'object on high shelf' or 'carrying a heavy object' (both 25.6%) contributed the most to the median overall score. The item 'putting on pants' yielded only a 2.6% contribution. After physiotherapy, the items 'from back pocket', 'putting on pants' and 'washing hair' no longer appeared, meaning that they yielded a median score of 0, a notable reduction.

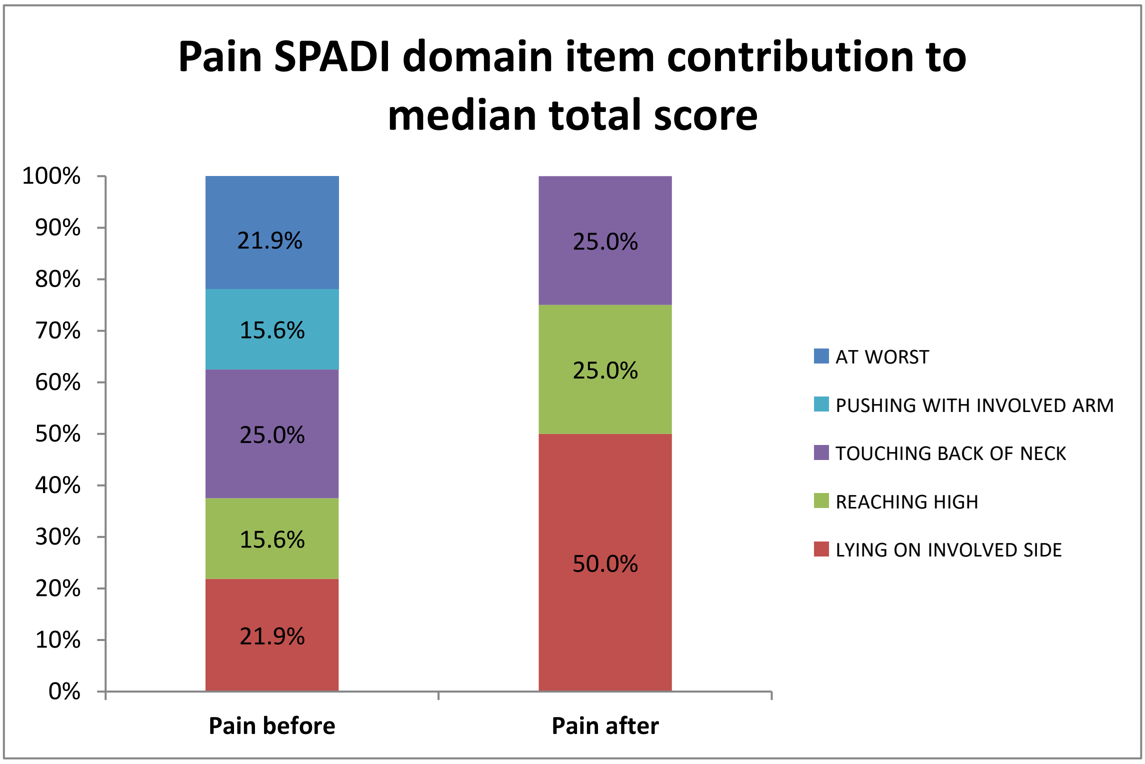


Figure 4.5. *The contribution of each item in the pain SPADI category to the median total pain score.*

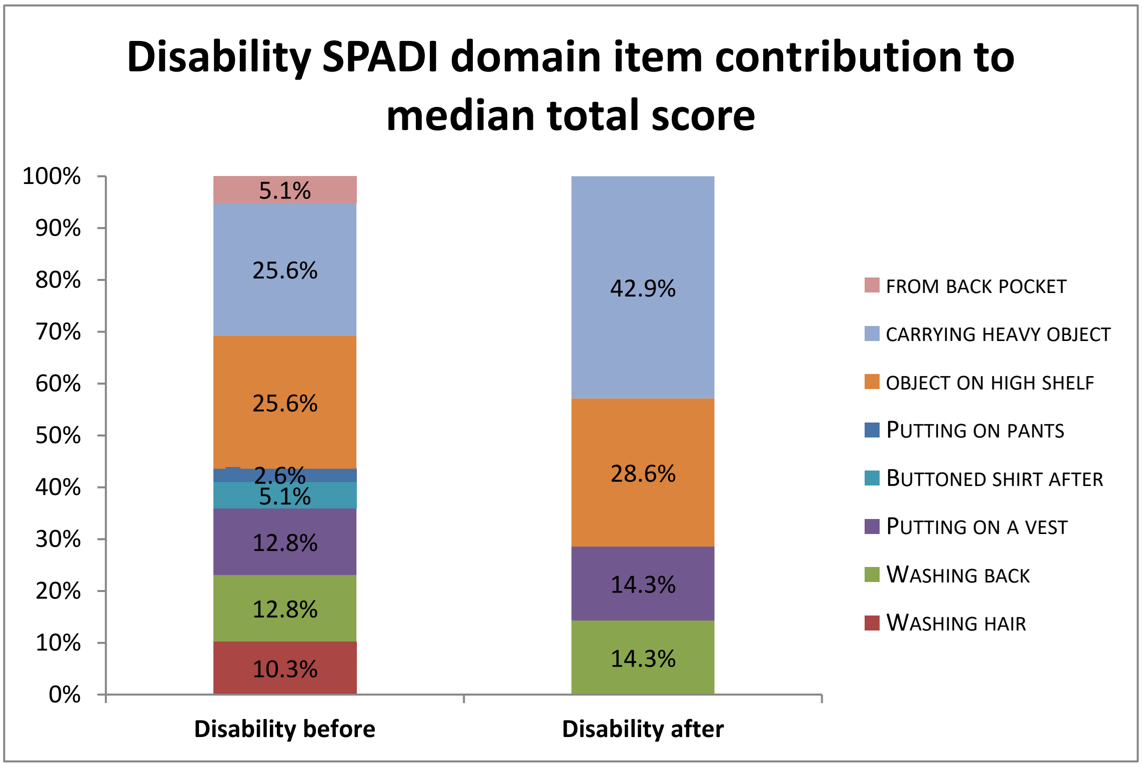


Figure 4.6. *The contribution of each item in the disability SPADI category to the median total disability score.*

4.5.4. FACT-B

4.5.4.1. Total FACT-B and domain scores

Figure 4.7 highlights the differences in median total FACT-B and component scores. The higher the total scores, the better the quality of life measure. The total scores were very similar with a score of 113 before physiotherapy and 112.25 after physiotherapy. Comparable scores were also evident in the subsection scores with only slight decreases in Emotional (2.5 points) and Social (1.75 points). Additional Concerns increased by 2.5 points and Functional increased by 1 point. The Physical median score remained the same. Item contribution scores total did not yield notable results.

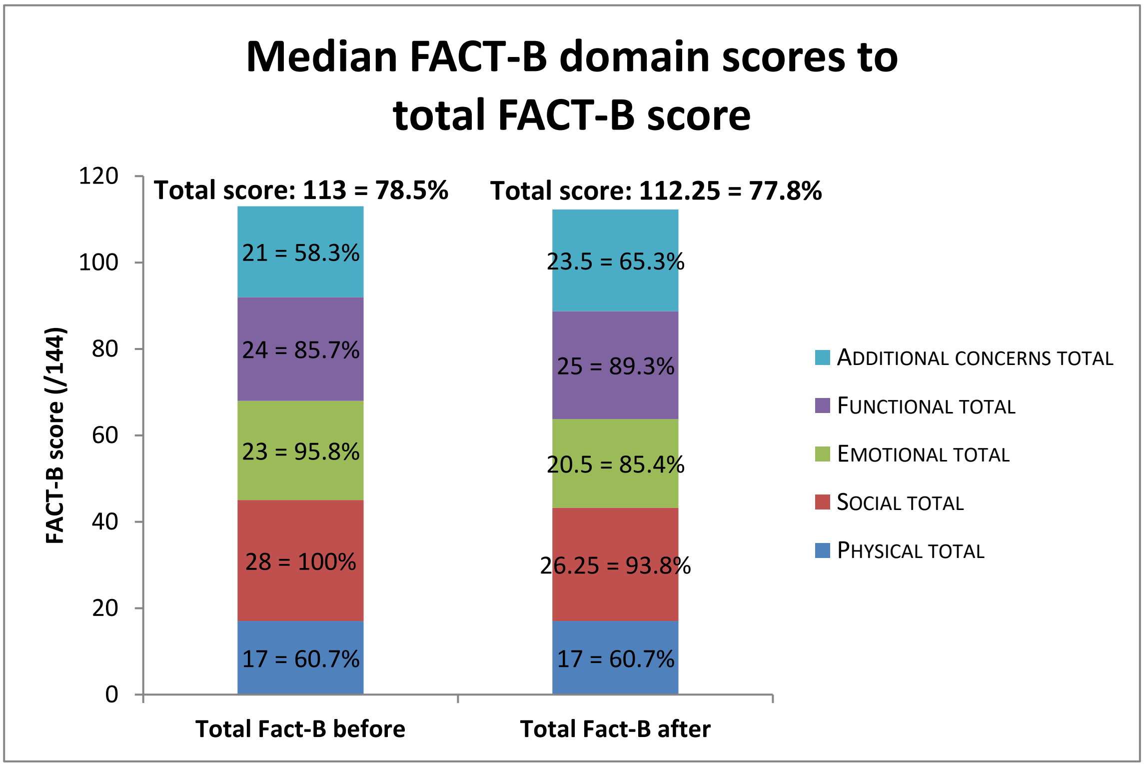


Figure 4.7. *The change in median total FACT-B score before versus after physiotherapy. The numbers inside the different subsections refer to the median score for that section. No statistically significant results were obtained (see Table 4.3).*

4.5.4.2. Percentage improvement Total FACT-B

Figure 4.8 shows the majority of patients having an improved FACT-B score except for FS/2013/08 with a reduction of 16.8%.

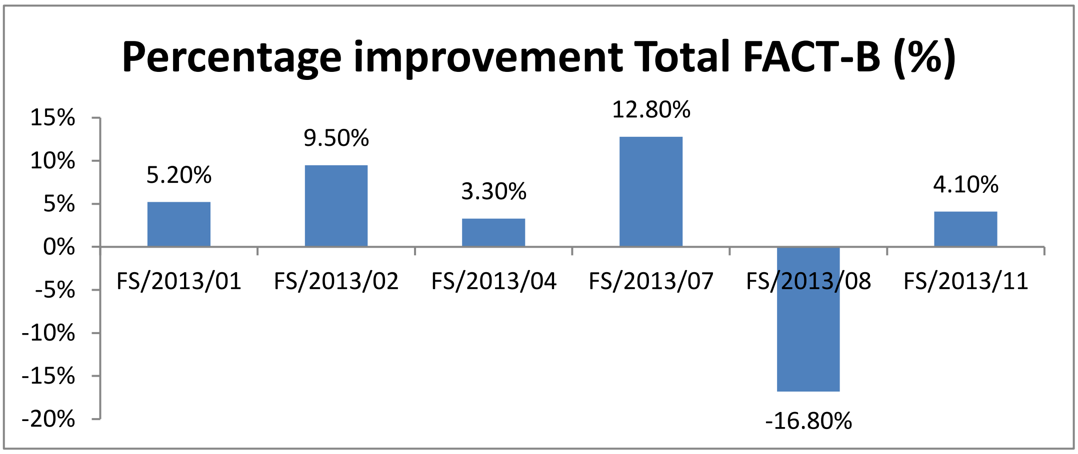


Figure 4.8. *Percentage individual improvement on the Total FACT-B score.*

4.6. General cord characteristics

The cord was fully exposed within the axilla with the patient's arm in abduction whilst standing or in the ABER position whilst lying down.

4.6.1. Cord position in axilla

Within the patient sample there was a variance in the cord location. The cord's trajectory did not perfectly follow the mid-axillary line as sometimes depicted, but also fell within the grooves between the musculature. The cord locations could be divided into three categories: (1) superior to coracobrachialis, (2) within the groove for axillary vessels, or (3) in the mid-axillary line (Figure 4.9).

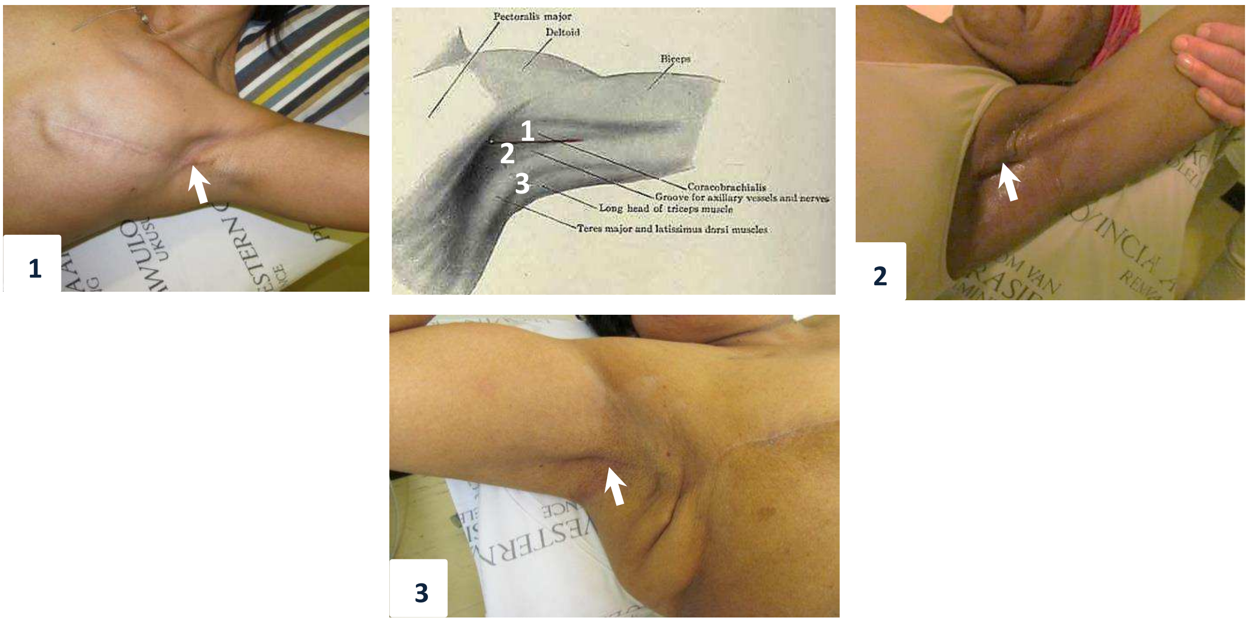


Figure 4.9. *Variance in cord location (arrows) corresponding to the anatomical diagram: (1) superficial to coracobrachialis, (2) in the axillary vessel groove, (3) in the mid-axillary line. Diagram adapted from* Applied Anatomy: The Construction of The Human Body *by Gwilym Davis (1913).*

4.6.2. Cord trajectory

In the current study's sample group, the cord's trajectory ranged from originating from the chest wall, the scar on the breast and the axilla, and ending in the axilla or upper limb, or extending towards the cubital fossa (Figure 4.10).

Figure 4.10. *Small cords extending over the cubital fossa.*

4.6.3. Webbing

Two patients had a second cord that was palpable but not clearly visible.

4.6.4. Cord thickness

The width of the cord varied from string-like structures to finger-thick cords (Figure 4.11).

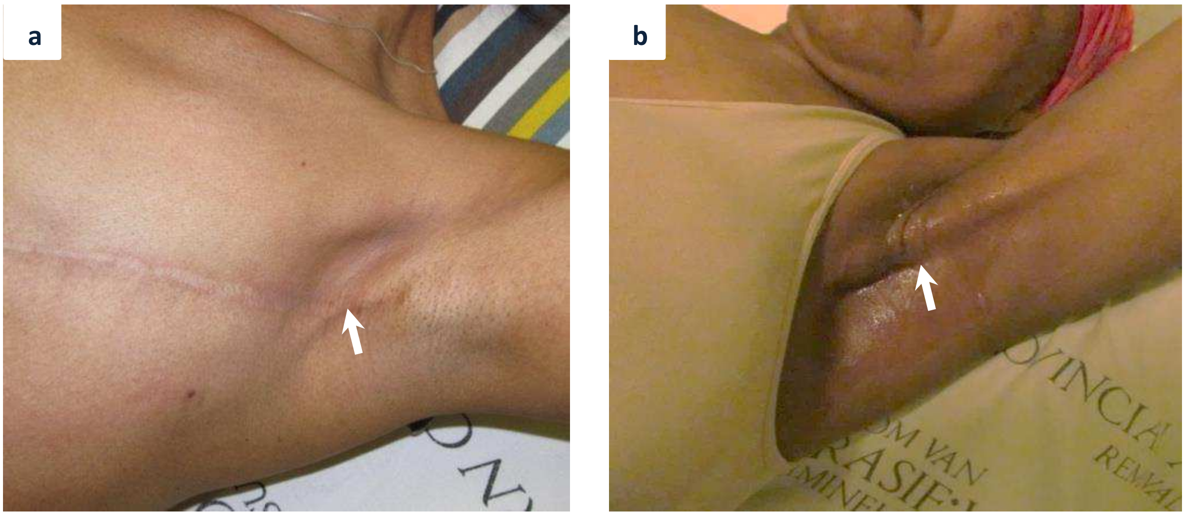


Figure 4.11. *The varying thicknesses of the cords: (a) a guitar-string cord and (b) a finger-thick cord.*

4.6.5. Length

The length of the cords was variable within our sample size and was defined as the length of the structure between its palpable and visible confines. It ranged from 57.96 mm to 139.52 mm before physiotherapy, and between 0 mm to 97.1 mm after physiotherapy.

4.6.6. Side

The cord appeared six times on the left side and seven times on the right side but was, on average, longer on the left side (median left: 100.3 mm versus median right: 81.9 mm) and both cord duplications appeared on the left side.

4.6.7. Appearance

Within the sample, two different presentations of the cord – both visible and palpable – were observed when the patient's upper limb was in the ABER position before physiotherapy: indenting (Figure 4.12a) and protruding (Figure 4.12b) cords. After physiotherapy cord presentation changed and was either resolved (Figure 4.13a) or a remnant was present (Figure 4.13b).

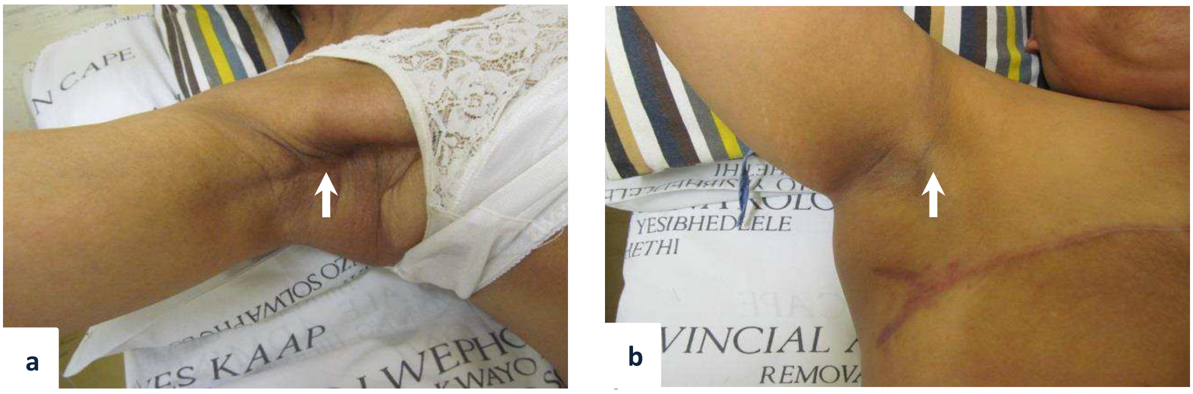


Figure 4.12. *Different cord appearances before physiotherapy: (a) indenting, (b) protruding.*

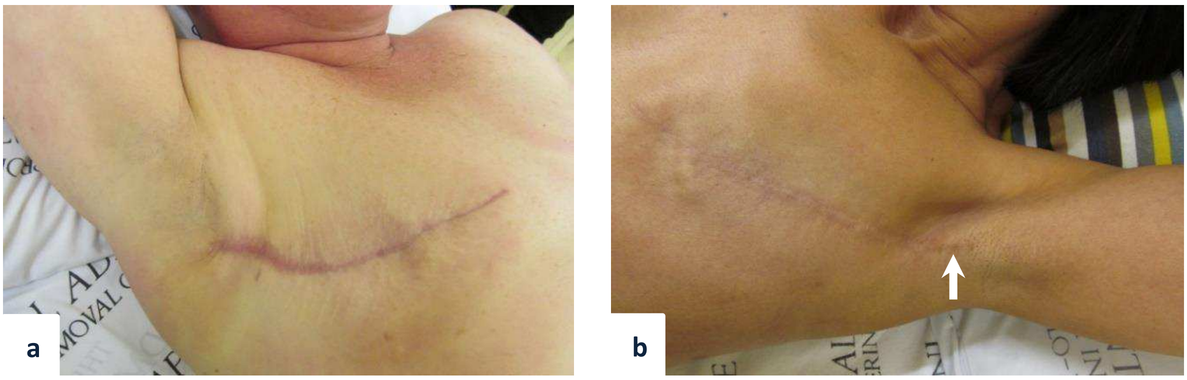


Figure 4.13. *Different cord appearances after physiotherapy: (a) resolved, (b) remnant present.*

4.7. General imaging findings

On the individual ultrasound (US) scans (Tables 4.5 and 4.6 per patient case; see Chapter 7 for more detail), a number of characteristics were observed to be present on the affected side compared to the unaffected side (Figure 4.14). Surprisingly, a clear cord structure was not noted in any of the patients. The characteristics observed were a thickened superficial fascia and deep fascia (Figure 4.14a), increased connections between the dermis and hypodermis as well as between the SF and DF (Figure 4.14a), (areas of) coarse homogeneity in the hypodermis or heterogeneity in echotexture (Figure 4.14b), general disorganisation in the hypodermis compared to the unaffected side (Figure 4.14c), reduced number of SF layers, the presence of a fibrous scar (Figure 4.14d), densification of the present layers, discontinuity of the layers, and arching of the skin and reduced gliding potential on the dynamic scans.

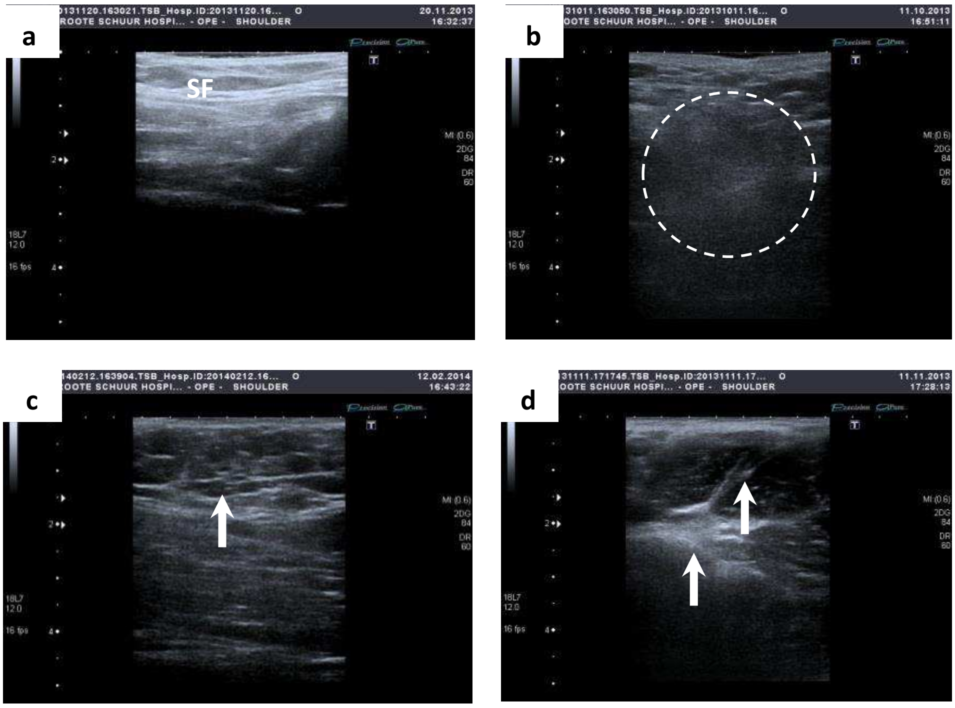


Figure 4.14. *Typical US findings in the present study: (a) highlights a thickened, dense, hyperechogenic superficial fascia (SF) with numerous extensions/adhesions to the skin; (b) highlights increased heterogenous echotexture (circle); (c) highlights tissue disruption and honeycomb structures (arrow); (d) highlights a fibrous scar extending to the tissue surrounding it and discontinuity of SF.*

The MRI scans of the single patient corroborate the US findings with the presence of adhesions arising from a fibrous conglomeration within the hypodermis stretching along the axillary wall, admixture of the fibrous tissue with adipose tissue in the hypodermis and connectivity of the band to surrounding deep fascia and muscles (Figure 4.15).

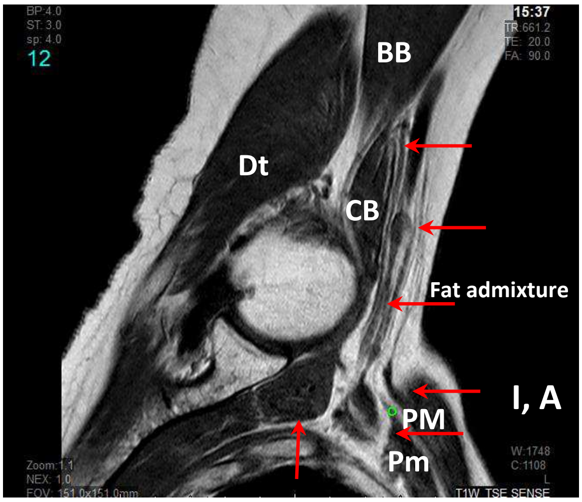


Figure 4.15. *Example MRI scan from patient 11. Long axis STIR PDFS T1 in parasagittal view showing fat admixture, fibrous bands indicated by the red arrow. For more MRI scans and a more detailed description, see Chapter 7. Orientation indicators: S=superior, I=inferior, P=posterior, A=anterior, L=lateral, M=medial. Within the scans: HH=humeral head, BB=biceps brachii, Dt=deltoid, CB=coracobrachialis, TM=teres major, LD=latissimus dorsi, PM=pectoralis major, Pm=pectoralis minor.*

4.8. General links between outcome measures and imaging

Tables 4.5 and 4.6 highlight each case's outcome measures and imaging findings as well as some demographic detail. A full analysis of each case and their individual differences, depending on the location of the cord, tightness and other symptomology, can be found in Chapter 7.

The case analyses show that the fascial differences as noticed on US imaging between affected and unaffected arms, and changes that presented after physiotherapy, agree with the findings in the other outcome measures. Improvements after physiotherapy generally showed decreased or absent cord length, improved ROM and reduced SPADI scores from baseline with decreased thickening of the fascial layers, decreased fascial connections between layers, decreased hyperechogenicity and freer and more fluid gliding on dynamic ultrasound scans. Descriptive correlation between the two imaging modalities in patient FS/2013/11 showed a concurrence in increased thickness of the fasciae which connected closely to the dermis and surrounding muscles.

Table 4.5. Summarised case histories of six patients with AWS who received physiotherapy, listing age, the side affected, treatments, time until recruitment, symptoms and confounding factors noted, ultrasound features, and ROM, SPADI and FACT-B scores.

Cases with physiotherapy								
Case number	**Age** (years)	**Side affected**	**Treatments** (see appendix for detail)	**Time until recruitment** (days)	**Self-reported symptoms** (before/after physiotherapy)	**Ultrasound features affected arm** (before/after physiotherapy)	**ROM** (% change after physiotherapy)	**SPADI and FACT-B** (% change after physiotherapy)
FS/2013/01	48	Both	**Surgery**: bilateral mastectomy, SLND (L), ANC (R) **Chemotherapy**: yes **Radiotherapy**: no **Hormonal therapy**: no **Physiotherapy**: x5	70	**Before:** cording, axillary and scar tightness, pain, reduced ROM **After:** none	**Before:** thicker and more dense homogeneous SF (L), honeycomb structures (R) **After:** more regularity, more fluid independent fascial gliding	**AFFECTED SIDE** (% change) **Abduction:** +78.1(L)/+130.1(R) **Extension:** +133.3(L)/+150(R) **Flexion:** +46(L)/+29.6(R) **Internal rot.:** +24.2(L)/+31(R) **External rot.:** +26.3(L)/+36.9(R)	**SPADI total:** -88.4(L)/ -65.7(R) **FACT-B total:** +5.1
FS/2013/02	38	Right	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: no **Physiotherapy**: x8	149	**Before:** cording, scar tightness, reduced ROM **After:** cord remnant (-65.4%)	**Before:** heterogenenous echotexture, hyperechoic bands in SF **After:** fewer clear connections SF to skin, coarser echotexture, improved gliding	**AFFECTED SIDE** (% change) **Abduction:** +47.8 **Extension:** +8.2 **Flexion:** -0.9 **Internal rot.:** -33.3 **External rot.:** -8.8	**SPADI total:** -75 **FACT-B total:** +9.5
FS/2013/04	69	Right	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes **Physiotherapy**: x6	368	**Before:** cording, pain, reduced ROM **After:** none ***Confounder:*** *thoracic kyphosis*	**Before:** increased disruption, thickened bands in SF **After:** more regularity and organisation, improved gliding	**AFFECTED SIDE** (% difference) **Abduction:** +48.9 **Extension:** +6.8 **Flexion:** +18 **Internal rot.:** +40.4 **External rot.:** -5.9	**SPADI total:** -36.8 **FACT-B total:** +3.3
FS/2013/07	63	Right	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes **Physiotherapy**: x5	798	**Before:** cording, pain, reduced ROM **After:** none ***Confounder:*** *thoracic kyphosis*	**Before:** thicker SF, disregularity, coarse echotexture **After:** more linearity and continuity of SF, decreased adhesions to dermis, improved gliding	**Abduction:** +97 **Extension:** +106.3 **Flexion:** +77.8 **Internal rot.:** +44.3 **External rot.:** +53.3	**SPADI total:** -41.2 **FACT-B total:** +12.8
FS/2013/08	68	Right	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: no **Hormonal therapy**: yes **Physiotherapy**: x6	1455	**Before:** cording, pain **After:** cording (+16%), pain ***Confounders:*** *longer time, fibromyalgia, no motivation for homework exercises, lower back pain*	**Before:** disorganisation in SF, increased thickening dermal-hypodermal junction **After:** more regularity, reduced connections	**Abduction:** +38.3 **Extension:** +7.8 **Flexion:** +28.3 **Internal rot.:** +27.4 **External rot.:** +500	**SPADI total:** -78.2 **FACT-B total:** -16.8
FS/2013/11	51	Left	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes **Physiotherapy**: x5	601	**Before:** cording **After:** cording (-69.7%)	**Before:** increased coarse echotexture, broken bands, increased connections to dermis **After:** more regularity and multilayering of SF, focal thickening still present	**Abduction:** +10.1 **Extension:** -11.3 **Flexion:** +16.7 **Internal rot.:** -24.2 **External rot.:** -11.8	**SPADI total:** -81.8 **FACT-B total:** +4.1

Table 4.6. *Summarised case histories of five patients with AWS who did not receive physiotherapy, listing age, the side affected, treatments, time until recruitment, symptoms and reason for drop-out from the study, ultrasound features, and ROM, SPADI and FACT-B scores.*

Cases without physiotherapy								
Case number	**Age** (years)	**Side affected**	**Treatments** (see appendix for detail)	**Time until recruitment** (days)	**Symptoms**	**Ultrasound features**	**ROM** (% difference compared to unaffected)	**SPADI and FACT-B**[#] (% of total possible score)
FS/2013/03	48	Left	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: no	132	Cording, pain, reduced ROM ***Drop-out****:* *socioeconomic factors*	Thickened and hyperechoic SF, layer adherence with reduced gliding, better continuity on unaffected side	**AFFECTED SIDE** **Abduction:** -89.3 **Extension:** +7.1 **Flexion:** -157.1 **Internal rot.:** -1.6 **External rot.:** -5.4	**SPADI total:** 82.3 **FACT-B total:** 67.9
FS/2013/05	35	Both	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: no **Hormonal therapy**: yes	201	Cording, pain ***Drop-out:*** *socioeconomic factors* ***Challenge:*** *language barrier*	Thickened and hyperechoic SF, adherence to muscles, greater organisation on unaffected side, fibrotic scar on both arms	**AFFECTED SIDE*** **Abduction:** 0 **Extension:** 10.2 **Flexion:** 3.4 **Internal rot.:** 23.4 **External rot.:** 1.8	**SPADI total:** 30.8 (L)/38.5(R) **FACT-B total:** 64.9
FS/2013/06	55	Right	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes	57	Cording, pain, reduced ROM ***Drop-out:*** *progressed illness*	Thickened SF, increased adherence to dermis, less organisation, adhesions between most layers, more defined and continuous on unaffected side	**AFFECTED SIDE** **Abduction:** +1.1 **Extension:** -71.9 **Flexion:** -14.1 **Internal rot.:** -53.7 **External rot.:** -425	**SPADI total:** 72.3 **FACT-B total:** 66.4
FS/2013/09	53	Left	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes	1122	Cording, pain, reduced ROM ***Drop-out:*** *socioeconomic factors*	Thickened and denser SF, reduced continuity, adherence to dermis, better organisation and regularity on unaffected side	**AFFECTED SIDE** **Abduction:** -51.2 **Extension:** -16.5 **Flexion:** -67.6 **Internal rot.:** +33.3 **External rot.:** -14.3	**SPADI total:** 74.6 **FACT-B total:** 55.4
FS/2013/10	48	Left	**Surgery**: mastectomy, axillary clearance **Chemotherapy**: yes **Radiotherapy**: yes **Hormonal therapy**: yes	1133	Cording, pain, reduced ROM ***Drop-out:*** *no response to call for physiotherapy*	Thickened and closely adherent SF, reduced continuity, better organisation on unaffected side	**AFFECTED SIDE** **Abduction:** -133.8 **Extension:** 0 **Flexion:** -18.9 **Internal rot.:** -19.6 **External rot.:** -56.9	**SPADI total:** 54.6 **FACT-B total:** 88.9

* The patient was affected on both arms and thus the ROM percentage difference is how much difference there was between the two affected arms.
[#] Note that a high SPADI score indicates more severe pain and disability, whereas a high FACT-B indicates better quality of life.

Chapter 5: Discussion

To facilitate an effective discussion, the discussion chapter will follow the structure of the hypotheses presented in the introduction.

The first hypothesis states that, "Altered fascia plays a role in the restriction of upper limb movement, the perpetuation of pain and the fibrosis and formation of the cord in axillary web syndrome (AWS)". The first aim of the first hypothesis was to descriptively relate variables that were found to be (risk) factors in the AWS literature to our study and the fascia literature to determine fascial involvement. The risk factor variables will be focused on in the subsections of Section 5.1 and in the cord characteristics in Section 5.2.2. The second aim was to test the use of ultrasound (US) as an imaging technique for fascia in AWS in patients after treatment for breast cancer and to observe whether findings on the ultrasonographs relate to the presenting symptoms complex.

The second aim as well as the second hypothesis, "Changes on US images of the cord, fascia and surrounding structures will be evident when the cord resolves, or symptoms improve", will be addressed in sections 5.2. and 5.3. when deliberating imaging and pre- and post-physiotherapy results.

Each topic and its link to fascia will be discussed using the characteristics found on imaging and with what is already known from the literature. Considering the relationship will aid in understanding the fascia from an anatomical and pathological point of view that may aid in explaining the relevant symptom complex and other variables in AWS. The sections that are discussed in the present chapter are demographic and treatment variables (Section 5.1.), AWS variables (Section 5.2.), physiotherapy (Section 5.3.) and limitations (Section 5.4.). The specific section from the results chapter to which a topic pertains is highlighted in the title.

5.1. Demographic and treatment variables

In the AWS literature, a number of demographic and treatment variables have been associated with symptom development and resolution. They are age (Section 5.1.1.), body fat and BMI (Section 5.1.2.), surgical treatment with cord formation, imaging findings, number of nodes removed, patient-dependent variables, time since surgery, cord resolution and definition of cord resolution (Section 5.1.3.), tumour variables (Section 5.1.4.) and (neo)adjuvant treatments (Section 5.1.5.).

5.1.1. **Age** (Results Section 4.2.)

Several authors have reported a relationship between age and AWS occurrence (Bergmann *et al.*, 2012; Koehler, 2013). The current study showed presentation over a wide age range (35 to 69 years) with a propensity towards those below 60 years (73% of the sample) which concurs with the literature (Bergmann *et al.*, 2012; Koehler, 2013). Although breast cancer occurrence and hence treatment tends to increase with age (McPherson, Steel & Dixon, 2000), an explanation for the phenomenon may be found in understanding the fascia and its healing.

Ageing affects the elastic fibres in the fasciae (Kirk & Chieffie, 1962). Changes that arise with age are a decreased number of fibroblasts and fewer collagen fibres that become disorganised, resulting in the skin losing its tension and becoming misshapen resulting in, for example, wrinkles (Abu-Hijleh, Dharap & Harris, 2012). A reduction in fibroblasts and fibres results in a reduced healing response and delayed scar tissue formation in the elderly (Engeland & Gajendrareddy, 2011), possibly making it less likely to develop cording.

Increased age has also been linked to a more rapid stiffening of the joints upon immobility (Findley, 2012) and there is evidence for range of movement (ROM) to be age-dependent (Barnes *et al.*, 2001) both possibly contributing to shoulder pain and reduced ROM in the older patients in the present study. Statistical analysis in the present study only showed a significant relationship between flexion and age after physiotherapy (r = -0.900) on the unaffected arm. The relationship indicates a reduced flexion in older patients which is supported by other studies (Doriot & Wang, 2006). That there was no relationship found on the affected arm could be explained by the altered dynamics due to the fascial changes having occurred (as will be discussed in Section 5.2.3.2.) possibly affecting both arms via direct connectivity and biotensegrity (see Section 5.2.3.2.1.) and after physiotherapy the unaffected arm having restored to more normal ROM. The lack of other correlations could be due to the small sample size of the current study and further studies would be required to examine the relationship between age, ROM and fascia in detail.

5.1.2. **Body fat and BMI** (Chapter 7 – Ultrasonography Section 4 per patient)

A relationship between a lower-normal body fat percentage and BMI has previously been correlated with the occurrence of cording (Lacomba *et al.*, 2009; Koehler, 2013). In the present study, BMI was not calculated; however, the thickness of the axillary hypodermis, which includes the SAT, SF and DAT, was measured on the US scans. Measuring the hypodermal thickness may be a better way to determine the adipose layer thickness in a localised area as BMI is an indirect measure of body fat and provides an average over the whole body (Rothman, 2008). The measurements showed a variety of hypodermal thickness from 0.1 cm to 2 cm in the axilla, ranging from thin to larger individuals with no clear descriptive propensity towards either.

The literature shows a mean BMI of 25.1 (Lacomba *et al*., 2009) and a mean of 24.8 (Koehler, 2013) in patients with cording. Bergmann and colleagues (2012) describe a decreased risk of 15% in obese patients. Leidenius and colleagues (2003) found that patients with AWS that do not have any symptoms are more likely to be obese (mean BMI = 26). O'Toole and colleagues (2013) and Leduc and colleagues (2009), on the contrary, did not observe a relationship between body fat or BMI and cording.

Lacomba and colleagues (2009) propose that the relationship might be related to increased adipose tissue decreasing the inflammatory reaction of the severed vessel, preventing fibrosis and cord formation. Koehler (2013) similarly hypothesises that the prevention of adhesion formation could be related to increased adipose tissue in the tissue healing response. Lacomba and colleagues (2009) relate their findings to age, in which they describe that older people are more likely to gain weight which could explain why AWS appears in younger and thinner women.

However, Leidenius and colleagues (2003) suggest a reason for the relationship could be that a cord might just not be observed or palpated easily in patients with higher BMI (>25) due to the thicker subcutaneous adipose layer. Additionally, Koehler (2013) suggests that in patients with lymphoedema the accumulated fluid might obstruct access and visibility to the cord, indicating a false relationship rather than a true one between BMI and cording. In the present study, an increased adipose layer did appear to mask symptoms of cording in patients with increased adiposity, making it difficult to clearly measure the extent of the cord or to discern it initially. Imaging modalities being able to visualise cording may be able to help identify cords in those patients with increased BMI.

5.1.3. **Surgical treatment** (Results Section 4.2. + 4.3.)

In the current sample, all patients underwent a mastectomy and received axillary surgery on the involved side and developed AWS symptoms on that side. The only exception was Patient FS/2013/05 who received a bilateral mastectomy and developed bilateral cording. The axillary surgery for the patients involved a full axillary clearance (ANC), except for patient FS/2013/01 who received a left mastectomy and sentinel lymph node dissection (SLND) and a prophylactic right mastectomy. Her right side, however, was also affected with AWS symptoms and showed a cord structure, although less obvious than on the left side.

In the literature, most studies describe axillary surgery as the main risk factor for developing AWS. In their seminal paper, Moskovitz and colleagues (2001) described that no patient in their sample developed cording with only a breast procedure without axillary surgery, only with axillary node clearance or sentinel lymph node dissection - which was mirrored by several others (Koehler, 2013; Lacomba *et al*., 2009). O'Toole *et al*. (2013), however, also reported four patients that had developed cords and had received breast procedures, but not axillary dissection.

Remarkably, other cases of AWS without axillary dissection were observed in the literature. A patient was described who developed axillary cording after a transaxillary thyroidectomy (Kim, Park & Gong, 2014) and one after an insect bite with secondary fungal infection (Friberg *et al*., 2013). In Moskovitz and colleagues' study (2001), one patient developed a cord on the side on which she developed stage IV fixed nodal disease. It was explained by the authors as tumour cells having occluded the lymphatic pathways and therefore giving rise to the cord.

An interesting observation is that, physiologically, the body forms fibrosed cords from occluded vessels; for example, to make redundant vessels non-functional. After birth the ductus arteriosus, which connects the aorta to the pulmonary trunk to shunt blood away from the lungs into the aorta during foetal development, constricts and fibroses in response to inflammatory markers to become the ligamentum arteriosum (Standring, 2008). To understand the formation of the cord in AWS, further research could focus on whether a similar process to that of the ductus is followed with similar biochemical markers. All the mentioned examples do point towards injury, dysfunctionality and inflammation of the axilla as the major factors involved in cord formation.

5.1.3.1. Cord formation

Moskovitz and colleagues (2001), in addition to others, propose that the webbed cord forms as a result of axillary surgery, hemisection of a vessel, extravasation of fluid and subsequent stasis and occlusion and fibrosis (Koehler, 2013; Lacomba *et al*., 2009). Cord formation can be explained through the wound-healing process as a consequence of the surgical insult and the removal of the axillary tissues.

An axillary clearance results in the removal of lymph nodes, axillary tissue and remnants of vasculature. The resulting cavity in the body undergoes a large inflammatory response and is initially filled with fluids but subsequently is reorganised (Panieri, personal communication, 2014). Guimberteau and Armstrong (2015) mention that the body works to avoid any unintentional cavities. The fibroblasts in the remaining fasciae aid in restoration and start depositing granulation tissue haphazardly to fill the cavity and re-establish tissue integrity

(Fourie, 2012). Adhesion formation as a consequence of cell breakdown and tissue reorganisation occurs within the deposited tissue and between other tissues (Fourie, 2014). In addition, the removal of lymph nodes causes the disruption of lymphatic and possibly other vessels and can lead to insufficient lymph drainage and lymphedema (Fumiere *et al.*, 2007) with a backing up of lymph fluid. The protein-rich fluid leaks into the interstitium and leads to fibrosis of the tissue and a damaged vessel wall to form the cord (Kepics, 2007). It may result in chronic inflammation and definitive fibrosis of surrounding tissues (Fumiere *et al.*, 2007). The inflammatory response that ensues after major surgery can thus explain the fibrosing of a damaged vessel forming a cord as well as the presence of generalised fibrotic tissue changes surrounding the cord.

Figures 5.1 and 5.2 show how tissue fibroses as a response to surgery. Figure 5.1 highlights the fibrosis that can occur post-injury and the destruction of the normal anatomy and functionality of the tissue. Figure 5.2 shows small vessels in fibrotic planes and adhesions as a result of long-term inflammation. The examples highlight how invasive surgical procedures may lead to the fibrotic tissue seen and felt in the AWS patients in the current study on clinical examination and can explain the arching of the skin (and different layers on the US) as a result of increased tension by pulling on the fibrotic fasciae upon movement. The puckered skin appearance can be explained by the SF that has elastic fibres, normally contributing to continuous endogenous tension on to the dermis (Standring, 2008), that are replaced by collagen, forming adhesions.

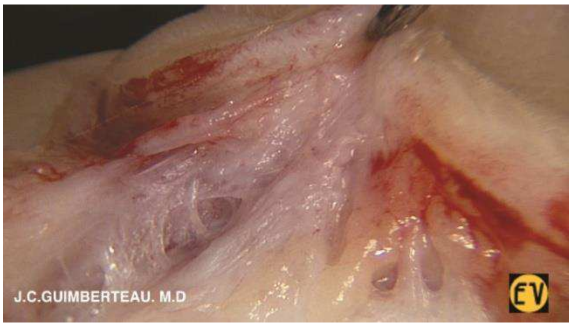


Figure 5.1. *Scar tissue after one year of injury showing the disrupted tissue, adhesions and fibrotic tissue below the skin. Photo courtesy of Jean-Claude Guimberteau, 2015.*

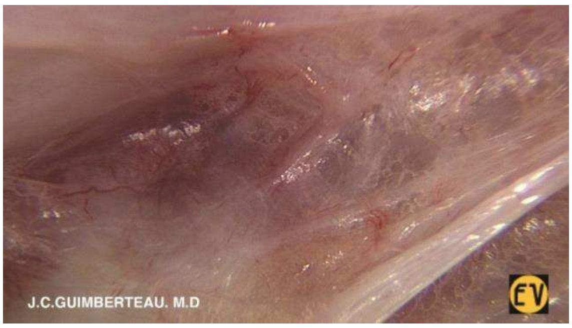


Figure 5.2. *The scar shows adhesions from the skin to the underlying aponeuroses with neovascularisation as a result of inflammation, highlighting the chronic inflammatory response responsible for the outcome. Photo courtesy of Jean-Claude Guimberteau, 2015.*

5.1.3.1.1. Imaging findings (Results Section 4.7.)

The fibrotic and adhesive features seen on imaging in the present study support the wound-healing explanation of cord formation. On US there was a reduced number of SF layers, general disorganisation in the hypodermis and loss of fascial continuity which may be explained by the disruption and removal of the axillary tissue following surgery as well as the resulting fibrotic response (Stecco, 2015). The irregular deposition of fibrotic tissue may explain adhesion formations between the dermis and SF as well as between the SF and DF on US and MRI (also observed by Fourie, 2012), and may explain the fascial thickening observed in the different layers. Leduc and colleagues (2014) also describe connections from the hyperechogenic fibrotic structure visualised on US to surrounding fascia and dermis. A fibrous scar as highlighted in some individuals in the current study was also highlighted on US by Fourie (2012).

Areas of coarse echotexture in the hypodermis as found in the present study were also described by Fumiere *et al.* (2007) as diffuse hypoechogenecity or localised hyperechogenicity in patients with lymphoedema. The authors explain that the appearance reflects water accumulation or diffuse fibrosclerosis, indicating a fibrosing response occurring. They found a good topographical correlation between hyperechogenic findings on US, hyposignal on MRI and invasive fibrosis on histology between and within adipocytes, similar to the US and MRI correlation of the present study. The histological fibrotic findings are reinforced by biopsy studies of the cord in AWS (Marcus, Pawade & Vella, 1990; Reedijk *et al*., 2006; Josenhans, 2007; Villamiel Capos *et al.*, 2008; Rashtak *et al.*, 2012). Coarse echotexture can be explained due to the admixture of adipose tissue which attenuates US and possibly masks or highlights the hyperechoic tissues and was also seen on MRI in the present study. Furthermore, the haphazard laying down of the tissue in the fibrotic response could also explain the hazy impression which has been described on US images of liver fibrosis (Perez *et al*., 2007).

Lastly, a honeycomb structure was found in the present study on US on the affected side of patients with cording, which was corroborated by a study by O'Toole and colleagues (2015). Although the structure of the axilla with its fibrofatty plugs and network of connective tissue surrounding the plugs could represent a honeycomb appearance (Stecco, 2015), the observed structure was especially evident in thickened tissues in the study. The structure also corresponds with the irregular microvacuolar polyhedral shapes forming microvolumes visualised by Guimberteau and Armstrong (2015) on intratissular endoscopy but were larger. The honeycomb appearance could be the result of normal fascial tissue having become congested with either fat, fibrotic tissue or fluid deposited during in the inflammatory process. Fumiere and colleagues (2007) suggest that the appearance may represent oedema as it appeared in patients with lymphoedema.

5.1.3.2. Number of nodes removed (Results Section 4.2.)

The number of nodes removed has been used by a number of authors as an indication of the invasiveness and extent of the axillary surgery and related to AWS development (Moskovitz *et al.*, 2001; Koehler, 2013; Bergmann *et al.*, 2012). In the present study, only one patient received an SLND, and the remainder full axillary clearances consisting of a median 12 nodes or more (over 90% of individuals had more than six nodes removed). When analysing the number of resected nodes, the number of resected nodes was significantly positively associated with age ($r = 0.847$). The correlation may be due to more nodes being removed prophylactically in older people and less conservative treatment, but was most likely coincidental due to the small sample size. The literature advices contrarily more conservative treatment for older patients with breast cancer as they do not benefit in terms of breast cancer mortality from axillary dissection (Martelli *et al.*, 2011). There was no statistically significant correlation with any of the AWS symptoms or descriptively with changes and differences seen on the ultrasonographs.

In the literature, both an increase in the number of nodes removed and more destructive surgery were found to predispose patients to AWS development, as increased tissue damage results in increased tissue fibrosis (Koehler, 2013). Leidenius and colleagues (2003) found that when patients underwent an axillary node clearance (> 5 nodes removed), there was a higher incidence of cording developing in 72% of patients, compared to 20% of patients after a more limited sentinel lymph node biopsy (SLNB). Moskovitz and colleagues (2001) reported a 6% incidence after ANC with preliminary results showing cord development after SLND, but no incidence was provided for the latter group. Koehler (2013) described a 4.8 times higher chance of developing cording with having 15 nodes removed compared to only two. Bergmann *et al.* (2012) describe an increased risk of 1% per node removed and in 2011 showed a reduced risk of 68% after SLND.

Using the number of resected nodes in the present study as the basis of extent of lymphatic disruption or invasion may not be a clear indicator of the true damage done. Panieri (personal communication, 2014) mentions that the number of lymph nodes counted is fully dependent on the skill and meticulousness of the anatomical pathologist. Since the lymph nodes vary in size from 1-2 cm to 2-3 mm the pathologist may sometimes quote the wrong number of nodes because nodes may be missed in the fibrofatty tissue. Determining the correct nodes is particularly important in a SLNB where one attempts to be as minimally invasive as possible and only remove the sentinel lymph nodes.

As mentioned before, the removal of more tissue leads to a worsened inflammatory response and a poorer outcome as tissues are less re-established to their original configuration if there is greater destruction (Guimberteau & Armstrong, 2015). Leidenius and colleagues (2003) point out that with current radiomarkers used to identify the sentinel lymph nodes, the colloid marker may leak out into the neighbouring nodes which could lead to unnecessary removal of too many nodes. Increased damage could predispose the patient to an increased inflammatory response and possible cording and should thus be addressed with future research on improved lymphatic markers (Leidenius *et al*., 2003). A better way to determine the extent of tissue damage may be to record the surgery procedure, the tissue removed and to follow the subsequent healing process.

5.1.3.3. Patient-dependent variables

A reason for the different rates of patients being affected with cord formation throughout the literature after breast cancer treatment could be related to patient-dependent variables that inform the surgical procedure. Panieri (personal communication, 2014) mentioned in an interview that, even though there might not be a formal axillary dissection done, the breast procedure often extends into the axilla to remove the full extent of the breast tissue which includes the axillary tail (Stecco, 2015). Furthermore, as the vasculature of the breast and axillary tissue share a common embryological origin and hence are closely connected (Moskovitz et al., 2001), disruption and fibrosis of the vasculature inferior to the axilla could possibly result in cording as seen in the present study in the patient who did not undergo formal axillary surgery.

Although surgery aims to follow a structured protocol and hence remain consistent in the removal of tissue, factors such as where incisions are made, how much tissue is removed (for example, the number of lymph nodes) and which tissues are damaged are reliant on the patient's body habitus and anatomical variation of the tissues to avoid and the tissue to remove (Panieri, personal communication, 2014). The present study showed that formal axillary dissection itself thus does not need to be a prerequisite for cord development. The current study was not able to investigate the exact anatomical details of which tissues were removed.

Additionally, depending on the stressors put on the injured tissue during the wound-healing process, a scar matures as a result of internal factors (inflammatory mediators) and external factors (functional strain) (Stecco & Stecco, 2012). Patient-specific variables may thus also alter the healing response (Van den Berg, 2012) and are further discussed in Section 5.1.3.4. In the present study, both types of factors may aid in explaining the differences found in cord presentation and appearance, and the variances found on US, even though all patients received a similar surgical treatment.

5.1.3.4. Time since surgery and cord resolution (Results Section 4.3.)

Several authors have proposed that AWS is a self-limiting disease that resolves within three months after symptom development and presentation (Moskovitz *et al.*, 2001; Rashtak *et al.*, 2012; Moreau *et al*., 2008; Lacomba *et al.*, 2009). In the present study, all patients presented with cording at the first observation point past the three-month cut-off time. There was a very wide range of number of days from surgery to the first measurement time with patients presenting with AWS from 57 days (±three months after surgery) to 1 455 days (± four years after surgery), of which six patients presented with cording more than a year post-surgery before physiotherapy. The syndrome did not appear to be self-limiting in the patients participating in the current study, highlighting that spontaneous resolution does not always occur. There are other studies that describe patients that do not follow the definitive timeline and present with symptoms more than three months and up to more than three years post-surgery (Johansson *et al*., 2001; Koehler, 2013; Leidenius *et al*., 2003; Fourie & Robb, 2009; Kepics, 2007; Wyrick, Waltke & Ng, 2006). If the syndrome is not self-limiting, the possible long-term effects of the syndrome are concerning and may be very debilitating (Cheville & Tchou, 2007).

The cord resolution that follows the three-month timeframe may be explained by the time taken for the tissue healing pathway to go through the stages of remodelling and scar tissue formation (Van den Berg, 2012). Injured tissue heals and remodels according to a triphasic healing cascade that takes place at specific time intervals: (i) the inflammatory phase (days 1-5) that prepares the injured area to heal, (ii) the fibroblastic phase (days 5-28) in which a scaffolding of collagen type III tissue which does not have great mechanical stability is laid down, and subsequently (iii) the reconstruction phase (days 28-365) in which the type III collagen tissue network gets replaced by type I collagen tissue (Fourie, 2014; Van den Berg, 2012). In the fibroblastic phase, the healing tissue requires physiological tension to attain the structure most resembling pre-injury condition (Cohen *et al*., 1992). However, scar tissue requires time to mature and if there are any irritating factors they may delay or disturb the maturation process and may lead to a chronic inflammatory process (Guimberteau & Armstrong, 2015) leading to non-functional scar tissue. The explained situation may explain the patients in whom cord resolution does not follow the three-month cut-off.

A number of factors that can intervene with the maturation process have been noted such as foreign body inclusion in the tissue, nerve hemisection, functional tension that is put on the skin too early, or excessive repair as in certain scar tissue disorders (Fourie, 2014). Factors that may be responsible for the findings in the current study may be that patients start using their arms too early after surgery, for example due to socioeconomic requirements, introducing a secondary or prolonged inflammatory response. The patients may also be anxious to use their arms for fear of hurting themselves and prolonged immobility could also lead to non-functional scar formation (Shultheis, Reichwein & Nebelung, 2012), to the extent that only surgery may then be able to release the tissues (Fourie, 2014).

Another explanation of the longer time since surgery and cording in the current study may be that there was more invasive surgery or inadequate or no rehabilitation compared to other studies – as there is a long waiting list in the public system in South Africa for physiotherapy treatment – or a patient's symptoms may be normalised after breast cancer treatment (Josenhans, 2007; Kepics, 2007) possibly worsening the symptoms. Increased physiological stress levels, inadequate nutrients and inadequate perfusion of the tissues have also been suggested to lead to poor healing and regeneration (Van den Berg, 2012), especially in a resource-constrained and socioeconomically disparate settings. The use of anti-inflammatory medication affects the inflammatory response poorly and affects the connective tissues as well (Van den Berg, 2012). Lastly, the use of analgesics post-surgery to aid in pain relief also remove the natural pain signal which may lead to overuse of the arms and result in a prolonged inflammatory response (Van den Berg, 2012). Caution is thus required in the use of pharmacological treatment.

5.1.3.5. Definition of cord resolution

If cord formation may be linked to a worsened inflammatory and fibrotic response, cord resolution may be explained by resorption of the fibrotic tissues. Cord resolution has, however, never been explicitly defined in the literature. Moskovitz and colleagues (2001) make mention of resolution of the cord as the self-limiting factor of AWS and appears to entail a disappearance of the webbed cord and accompanying symptoms so that one cannot visually observe or palpate it. What happens to the physical cord structure upon resolution is unclear.

The ligamentum arteriosum may be thought of as an example of a cord, exemplifying that a fibrotic vessel may not get completely resorbed (Standring, 2008). A different explanation for how the cord becomes unobservable is that the adhesions that keep the structure adherent to the skin and superficial tissues are resolved over time, or broken, allowing the fibrotic vessel to become buried within the surrounding tissue.

The breaking of the adhesions tethering the cord could explain the "popping" sound which is reported by our physiotherapist occurring in two patients in the current study during her treatment, and was previously reported by manual therapists to occur after myofascial release in other studies (Fourie & Robb, 2009; Lattanzi, Zimmerman & Marshall, 2012). In the current study, adhesions were visualised on the US and MRI scans between the skin and superficial fasciae in most patients and were less obvious post-physiotherapy. The same patients presented with immediate improvement in pain and range of movement and reduced cord length after physiotherapy treatment.

Furthermore, reports of recurrences of the cord can explain the adhesion hypothesis as well. After adjuvant, invasive treatment some patients re-presented with cords (Lacomba *et al.*, 2009) which could be explained by a reignited inflammatory response and fibrotic tissue formation. In the current study, patient FS/2013/02, who received radiotherapy during the physiotherapy cycle, presented with worse cording and tighter and more adhesive skin afterwards.

5.1.4. **Tumour variables** (Results Section 4.2.)

The size, type and location of the breast cancer tumour in AWS patients may have an additional impact on the healing process as recent discussions in the literature point out. Topical cancer biological studies highlight that the connective tissues play an important role in the immediate tumour environment (Stamenkovic, 2000). The tumour can cause tissue damage by releasing proteolytic enzymes (Stamenkovic, 2000), distorting the tissue anatomy (Laug, DeClerck & Jones, 1983) and causing the release of TGF-B and fibrinogen which leads to collagen deposition and fibrosis (Dvorak, 1986). The tumour can be seen as an inflammatory process and produces inflammatory responses to the surrounding tissues leading to the adhesive tissue that forms part of the tumour (Stone *et al.*, 2003). The fasciae themselves also appear to contribute to cancer growth via the factors they release in fibrosis and inflammation (Langevin *et al.*, 2016). The inflammatory response following the removal of the cancer may thus be exaggerated due to the presence of local inflammatory factors in especially larger and higher grade/stage cancers.

In the AWS literature, the link between tumour size creating a pro-fibrotic environment and worse cording has not been explored but warrants future examination. Although there were clear fibrotic changes on US in the current study, no link could necessarily be made to the tumour size as being a determining factor as patients with the biggest tumour (> 80 mm) were not observed to have thicker, more disrupted fascia or more adhesions than those with smaller tumours. Statistical analysis did not show any correlation between other variables either. Furthermore, the variation in location (e.g. in the breast versus cancerous tissue in the axilla), and type of tumour, makes the relationship difficult to examine in our small sample. However, a contribution to the fibrotic findings and cord formation should not be ignored. A clearer effector of fibrosis is the (neo)adjuvant treatments they received.

5.1.5. **(Neo)adjuvant treatment** (Results Section 4.2.)

Radiotherapy, chemotherapy, hormonal therapy and other inflammatory inducing agents or triggers such as the cancer itself and infection lead to initiating a healing response (Fourie, 2014), affecting the connective tissues. The healing response includes the production of cytokines such as TGF-B which has been shown to be involved in stimulating fibroblasts to produce collagen with over-activation resulting in fibrosis (Van den Berg, 2012). Furthermore, leakage of fibrin also encourages collagen production and deposition, further contributing to the fibrotic response (Stone et al., 2003). Table 5.1 indicates the different points in time at which the patients in the study received the different adjuvant therapies. The table highlights how many treatments each patient obtained which, together with the timing, could indicate an effect on the healing response that could explain the fibrotic findings and cording present.

Multiple treatments appear to compromise healing due to the continued activation of the healing cascade (Stone *et al.*, 2003). Stone and colleagues (2003) described that using chemotherapy and radiotherapy simultaneously could lead to a worse fibrotic response and that pre-surgery radiotherapy can initiate fibrosis and tissue breakdown more quickly after surgery (Stone *et al.*, 2003). Systemic treatments such as chemotherapy and hormonal therapy could thus affect and worsen local inflammatory responses resulting from surgery and radiotherapy. Furthermore, Lacomba and colleagues (2009) describe recurrences of AWS in patients for whom the cord had resolved but reappeared post-adjuvant therapy.

In the present study, one patient received chemotherapy only, two patients received chemotherapy and radiotherapy, two patients received chemotherapy and hormonal therapy, and the other patients received all three treatment options. No correlation could, however, be found between having multiple treatments and having more reduced ROM or higher SPADI score. Also, due to the limited sample size of patients and that they received a myriad of different treatments at different times, prevented the authors from performing formal risk factor analysis (Table 5.1). Ranking was attempted to appreciate the effects of the different treatments but was inconclusive (Appendix I). Similarly, US findings could not be clearly attributed to the treatments; the US results, however, could have been worsened by the different treatments they received. Each treatment will now be discussed to elaborate on their effects on fasciae.

Table 5.1. *Points in time of (neo)adjuvant therapy relative to the surgery*

Time of (neo)adjuvant treatments relative to surgery			
Participant #	**Radiation therapy**	**Chemotherapy**	**Hormonal therapy#**
FS/2013/01	-	2x Post (extending into physio)	-
FS/2013/02	1x Post (extending into physio)	1x Post/ 1x Post (extending into physio)	-
FS/2013/03	1x Pre**	1x Pre*/ 1x Post	-
FS/2013/04	1x Post	1x Post (extending into physio)	2x Post
FS/2013/05	-	2x Pre*	1x Pre**/ 1x Pre
FS/2013/06	1x Pre*/ 1x Pre**	1x Pre*/1x Pre	1x Pre*/ 2x Pre**/1x Post
FS/2013/07	1x Post	1x Post**	1x Post**
FS/2013/08	1x Post^	2x Post**	1x Post*/1x Post*
FS/2013/09	1x Post***	1x Pre**	1x Post**
FS/2013/10	1x Post*	1x Post**	1x Post*/1x Post***
FS/2013/11	1x Post**	1x Post**	1x Post**

Bolded participants are those that finished the study; the patients in red all had all three treatments

Due to an inability to extract the end-date of the hormonal therapies from the patient folders, we were unable to determine whether the patients were taking the medication during our study

* Treatment occurred one year or longer (late effects) from the date of surgery and the first measurement cycle

** Treatment occurred one year or longer (late effects) from the date of the first measurement cycle; less than one year to the date of surgery

*** Treatment occurred one year or longer (late effects) from the date of surgery; less than one year to the date of the first measurement cycle

^ The radiotherapy data for the patient could not be found in her patient file

5.1.5.1. Radiotherapy

Irradiation of tissues with ionising beams during radiotherapy leads to damage of both malignant and surrounding tissues and subsequent activation of the inflammatory cascade (Stone et al., 2003). How a tissue tolerates the ionising radiation depends on the functional reserve and structural organisation of the tissues (Stone et al., 2003).

Radiation injury can be classified according to (i) immediate or acute effects where damage appears immediately, (ii) consequential after effects where there is persistent tissue damage and (iii) late effects which occur from approximately one-year post treatment (Stone *et al.*, 2003). Acute effects are predominantly seen in rapidly-dividing cells and skin cells, for example, and get replaced, whereas late effects show more increased tissue damage and lead to a worse inflammatory response. Similarly, chronic damage due to continuous activation of the healing cascade results in consequential late effects. The consequential late effects are often observed in combination therapies which results in fibrosis, adhesions and lymphoedema in the skin due to fibrinous exudate and collagenous deposition, and highlight injury to connective and vascular tissues (Stone et al., 2003).

Fractionating treatments determine some of the outcome of the effects. Larger dose fractions require less total dose but lead to more long-term effects; conversely, smaller fractions require a larger dose but have fewer long-term effects (Stone *et al*., 2003). All patients in the present study with smaller doses were shown to reduce late effects and have less severe outcomes. Patient FS/2013/02 received the largest dose per fraction of 3.2 Gy compared to 2.4-2.7 Gy for the other patients and received a second radiotherapy treatment during the physiotherapy treatment, which led to her having to stop the physiotherapy treatment and restart a few weeks later with worsened symptoms as described in the physiotherapy notes and patient cases.

The worsened symptoms in patient FS/2013/02 could be the result of more severe consequential late effects to the fascia and other tissues, exacerbated by chemotherapy (Stone *et al*., 2003) and could also account for the reduced improvement after physiotherapy (< 20% improvement on ROM taking into account the baseline she had), limited changes on US (residual increased echotexture) and a cord remnant present. The specific patient example agrees with the literature on the effect of radiotherapy. Generally, a trend appeared that those treated with radiotherapy appeared to have a greater amount of fibrosis as visualised on US in the form of coarse echotexture and thickened fascial layers, which has been identified in the literature (Stone *et al*., 2003).

5.1.5.2. Chemotherapy

Apart from having fibrotic effects, chemotherapy drugs have also been shown to increase radiosensitivity of certain tissues (Stone *et al*., 2003). Table 5.2 indicates the different treatments the current cohort of patients was exposed to and the evidence in the literature on whether they have been shown to be implicated in fibrosis or lead to increased sensitivity to injury and subsequent fibrosis after radiotherapy. All regimens and drugs used in the cohort appear to lead to increased sensitivity of certain anatomical tissues with direct evidence showing cyclophosphamide causing lung fibrosis (Yu *et al*., 2004). Little evidence could be found in the literature for the effects of chemotherapy on skin and subdermal tissues, except for paclitaxel and docetaxel which have been shown to be involved in cutaneous fibrosis (Cleveland, Ajaikumar & Reganti, 2000; Ostoros *et al*., 2006). 5-Fluoroacil, as part of most drug regimens given to patients in the current sample (Table 5.2), has been suggested to reduce proliferation of myofibroblasts (which have a contractile function in the fasciae), but this conjecture was not supported in experimental studies (Bulstrode *et al*., 2005). On the other hand, the same paper does point to lung fibrosis sharing a relationship with 5-fluoroacil treatment.

In the current study, a direct contribution of chemotherapy was possibly only observed in patient FS/2013/02. She received one chemotherapy cycle (with CEF) and started a second (with paclitaxel), as well as her radiotherapy treatment during physiotherapy, possibly affecting her outcomes of increased axillary fibrosis and adhesions as observed by the physiotherapist.

Chemotherapy has also been linked to altered shoulder movement in a study done by Shamley and colleagues (2012) in which breast cancer patients showed decreased activity in pectoralis major and increased activity in serratus anterior. Decreased activity in the muscles leads to movement deviations and possible worsened outcomes, and may be a contributing factor to the results found in the current study.

Table 5.2. *A summary of the different chemotherapy drugs administered to the study participants and whether they have been shown to effect fibrosis, and their anatomical locations, with example studies.*

Chemotherapy drugs and fibrosis			
Name	**Constituents**	**Fibrosis**	**Anatomical location**
CAF	Cyclophosphamide*	Y	Pulmonary – pleura (Yu *et al.*, 2004)
	Adriamycin#		(Lee & Harris, 2011)
	5-Fluoroacil#		(Bulstrode *et al.*, 2005)
CEF	Cyclophosphamide*	Y	Pulmonary – pleura (Yu *et al.*, 2004)
	Epirubicin		-
	5-Fluoroacil#		(Bulstrode *et al.*, 2005)
Paclitaxel	-	Y	Pulmonary – alveoli, interstitial; Cutaneous (Ostoros *et al.*, 2006)
Gemcitabine#	-	Y	Pulmonary – alveoli, interstitial; liver (Shahrokni *et al.*, 2007)
CMF	Cyclophosphamide*	Y	Pulmonary – pleura (Yu *et al.*, 2004)
	Methotrexate#	Y	Pulmonary – alveoli, interstitial (Bedrossian *et al.*, 1979)
	5-Fluoroacil#		(Bulstrode *et al.*, 2005)
Vinorelbine#	-	Y	Pulmonary – alveoli (Kirkbride *et al.*, 2002)
Taxotere/Docetaxel#	-	Y	Diffuse scleroderma (Hassett *et al.*, 2001) Cutaneous (Cleveland *et al.*, 2000)

radiation-sensitizing agents
* causes lung fibrosis
Y = yes, N = no

5.1.5.3. Hormonal therapy

Tamoxifen was the only hormonal therapy that was found in the literature to be related to fibrosis; in particular, enhancing the fibrotic effects of radiotherapy treatment to the lungs (Table 5.3), but could also have further reaching effects. As an aromatase inhibitor, it reduces the amount of oestrogen circulating in the body to reduce the growth of oestrogen-sensitive tumours (Fede *et al.*, 2016). Recent discoveries have shown sex hormone receptors to be present on fascial tissue and that oestrogen has an anti-fibrotic effect on the receptors by reducing TGF-B expression and collagen deposition (Fede *et al.*, 2016). Less oestrogen, as a consequence of taking tamoxifen, could thus lead to more fibrosis. The finding has been used to explain the observation that women experience more fibrosis and myofascial pain than men (Fede *et al.*, 2016), and could explain a contribution of the drug to the fibrotic findings found in the current study.

Table 5.3. *A summary of the different hormonal therapy drugs administered to the study participants and whether they have been shown to cause fibrosis, and their anatomical locations, with example studies.*

Hormonal therapy drug and fibrosis		
Name	**Fibrosis**	**Anatomical location (study)**
Arimidex/Anastrasole	N	(Yavas *et al.*, 2013)
Tamoxifen	Y	Pulmonary – alveoli, interstitial; liver (Yu *et al.*, 2004)
Exemestane	-	-
Provera	-	-

5.2. AWS variables

The majority of the sections in the previous section were able to be explained using fascial terminology – supporting the first hypothesis of the present study. The current section highlights general findings (Section 5.2.1) and findings regarding patient symptomology in AWS and fascial explanations where appropriate. In order of discussion are: pain (Section 5.2.3.1.), ROM (Section 5.2.3.2.) and FACT-B and quality of life (Section 5.2.3.3.)

5.2.1. General (Results Section 4.3.)

In the literature, the main symptom triad of AWS is described as cording, pain and reduced movement with a feeling of tightness. The symptomology presented by patients in the present study showed that not all patients complained of reduced ROM (n = 3) and two did not complain about having pain. The pathognomonic sign therefore appears to be the axillary cord, with which the literature agrees (Moskovitz et al., 2001; Tilley, Thomas-MacLean & Kwan, 2009; Rashtak et al., 2012; Craythorne, Benton & Macfarlane, 2009). The literature divides the cases into symptomatic or asymptomatic; why some patients remain without symptoms is not explained (Yeung, McPhail & Kuys, 2015). The differences in presentation in the literature could be due to individualising factors in treatment, as highlighted by the variability in cord and symptom presentation in the current study.

Some studies include numbness as an additional symptom (Wei *et al.*, 2013; Lattanzi, Zimmerman & Marshall, 2012) possibly because of intercostobrachial nerve involvement and damage either during surgery (Cheville & Tchou, 2007) or impingement subsequently.

Symptom resolution did appear in most patients in the current study after physiotherapy (including cord resolution as described above), but some patients still reported continuing tightness and pain. The continued presence of some symptoms in our sample corresponds with the literature as especially limited shoulder ROM was still present in patients, even if the other symptoms resolved (Craythorne, Benton & Macfarlane, 2009; Wei et al., 2013).

5.2.2. Cord characteristics

The present section highlights specific surface anatomical characteristics of the cord an factors influencing it. In the order they are discussed below are cord length (Section 5.2.2.1.), multiplicity (Section 5.2.2.2.), location and extension (Section 5.2.2.3.), size and grading (Section 5.2.2.4.), and cord appearance (Section 5.2.2.5.).

5.2.2.1. Cord length (Results Section 4.2. + 4.4.2. + 4.6.5.)

The present study is one of few that has looked at cord length. In our current sample, the cords, as measured in the axillary space, ranged from 5.7 cm to 14.0 cm before physiotherapy and from 0 cm to up to 9.7 cm in those in which the cord did not resolve after physiotherapy, which was not a statistically significant change. The cord did, however, resolve in 50% of the sample. Koehler (2013) describes that, in a sample of 17 patients, the cord length ranged between 0.3 cm and 17.2 cm. Leduc and colleagues (2009) describe a longer cord length in his 15 patients with a range of 24 cm to 57 cm, but was able to follow it beyond the axillary space. The discrepancy between the studies might be because of different measuring methods and definitions, individual characteristics that may worsen the cord development and presentation such as anatomical variation of the affected vessels and tissues resected, adjuvant therapies used, an inability to measure the cord due to an inability to hold the arm open, or may be related to BMI, making the cord easier to observe beyond the axilla.

Further analysis of the cord length and relating it to other outcome variables in the present study showed a single statistically significant relationship before physiotherapy between increased internal rotation and a longer cord length (r = 0.791). The relationship may be explained by the observation that the longer the cord length, the more exposed the cord is. In the majority of patients, the cord appears to be attached mostly in the midaxillary line impeding predominantly abduction movements as that is where the tension is placed, and tissue glide is therefore restricted (as seen in the current study). Internal rotation puts more tension medially, allowing the axilla to open up and the arm to move more easily, especially for a longer cord in which the attachments may be closer to the skin given the definition in the current study of cord length being the length between the outermost points of tethering.

After physiotherapy, there was a significant negative association between cord length and SPADI Pain (r = -0.895). The relationship could be explained by hypothesising that, the longer the cord the more adhesive tissue will have formed, and hence the more fascial pathology will be present including the increased activation of nociceptors (also see Section 5.2.3.1.2.).

Generally, decreased cord length appeared to descriptively relate to better SPADI scores and ROM. Individual improvements, as seen in the case reports, highlighted the improvement in all domains after physiotherapy and cord length reduction or resolution. Better functioning is corroborated by the findings by Fourie & Robb (2009) which showed improvement in ROM and pain upon cord resolution.

Cord length may not, however, be a good indicator of the true size of the full lesion as the cord is thought to be the area where the fibrosed vessel is adherent to the dermis via adhesions (Fourie, 2014) and an external measure may thus not be clinically relevant. For example, in the current study, cord length after physiotherapy was found to be reduced and accompanied by reduced restriction, tightness and adhesions of several layers to the dermis on US. A study by Fourie & Robb (2009) found similar findings and explained it by their loosening of the cord from its skin adhesions using manual therapy. Furthermore, the full extent may not be visible due to the difficulty observing the cord on US (Leduc *et al.*, 2014). The inability to visualise the cord fully indicates that it might be only visible and palpable cord disappearance and not real shortening of the lesion in the studies where the cords have resolved as has been discussed in Section 5.1.3.5.

5.2.2.2. Multiplicity (Results Section 4.6.3.)

Multiple axillary cords, or webbing, is the reason for which AWS got its name. In the present study, only one patient described having two cords, the second of which was not very clearly observable. Numerous studies describe not one but multiple cords appearing in the axilla (Leduc *et al.*, 2009; Koehler *et al,* 2014). If one observes that the cords are fibrosed vessels that were damaged during axillary surgery, the occurrence of multiple cords may be the result of either multiple vessels being damaged or an injury at a vessel that bifurcates leading to the multiple fibrosed strands. The superficial fascia in the axilla contains venous and lymphatic plexi that could be the target of the damage (Standring, 2008).

5.2.2.3. Location and extent (Results Section 4.6.1. + 4.6.2.)

The exact location of the cord in the axilla had not yet been documented in the literature prior to the current study. The present study found cords appearing either superficial to coracobrachialis, in the axillary vascular groove or in the mix-axillary line (Figure 4.27) and only one patient presented beyond the axilla reaching over the cubital fossa (FS/2013/01).

Koehler (2013) described the cord's presence in predominantly the axilla, but also in the upper arm, elbow, forearm and chest wall. Leduc and colleagues (2009) described the cord as arising from the axilla and course via the epitrochlear area, via the anteromedian aspect of the forearm to the base of the thumb in all the patients in his sample. The finding of Leduc and colleagues (2009) contrasts to our study, as they showed the majority of the cords originating from the lower axilla, often arising from the scar, and then disappearing in the proximal upper limb or axilla.

The location of the cord may give an indication of the anatomical origin of the cord. A study by Leduc *et al*. (2009) attempted localisation of the cord to identify the anatomical structures involved, comparing the trajectory of the cord along the upper limb to cadaveric specimens of the superficial lymphatic pathways which overlapped. The present study was unable to localise the cords beyond the axilla due to most of the cords' trajectories being limited to the axilla. The current study did show the majority of the fascial changes occurring close to the dermis on US, indicating that small lymphatic vessels or veins present in the SAT may be implicated as that is their anatomical location (Stecco, 2015). The small size of the vessels, however, does not necessarily corroborate the external appearance of some very large and thick cords, and some very thin, and will be discussed in the next section. Determining the anatomical origin of the cord was beyond the scope of the current study and future research using biopsy studies may be more successful.

5.2.2.4. Size and grading (Results Section 4.6.4.)

Grading the size of the axillary cord has not been done in a standardised fashion in the literature (Yeung, McPhail & Kuys, 2015). In the present study, it proved difficult to measure the cord's diameter due to its variable width along its length and the inability to measure accurately; hence, descriptive terms such as string-like and finger-thick were used and a variety of presentations were observed that were not able to be linked to findings on other domains per se.

Other studies attempted to standardise measurement of the thickness by using different methods. Josenhans (2007) described the width of a cord using a scale that ranged from '+' being a small cord and '+++' indicating a thick cord. Koehler (2013) described it as 1 mm, bigger or smaller than that. She did, however, indicate the same difficulty of measurement with callipers due to the cords being too deep or not visible or having increased hypodermal thickness.

A thickness measure, however, may be artificial as it will include surrounding tissues of the fibrosed vessel structure such as superficial adipose and fibrous tissue and may not be what, in the literature, is understood as the cord. The variable thicknesses along the length of a cord as observed in the study may corroborate that. As previously mentioned, a clear definition of exactly what the cord is has not been discussed; the definition needs to clarified in further studies. For the purposes of the present study, the cord includes the full extent of the fibrosity and is not limited to a fibrosed vessel.

5.2.2.5. Cord appearance (Results Section 4.6.7.)

Cord appearance has been described in the literature on the basis of whether the cord was visible (protruding) and showed a clear bowstring appearance or whether it was only palpable – which presented almost 50% each in a study by Leidenius *et al.* (2003) – which adds to its elusive character and could be related to BMI or hypodermal thickness.

In Mondor's disease, where the cords appear similar to the cords in AWS but in a different location, a relationship in the appearance of the cord, which either indents or protrudes, and the hypodermal thickness, was observed (Bauerfeind, Himsl & Rueh, 2006). A patient with more adipose tissue would present with a furrow and can be explained by adipose tissue accumulating around the cord pulling the skin inwards. A number of cases with Mondor's disease presenting on the lateral side of, and superior to, the breast and on the chest wall exemplified the furrow appearance (Bauerfeind, Himsl & Ruehl, 2006). In our present sample, however, few patients exhibited a relationship to hypodermal thickness with some patients presenting with a 2 cm thick hypodermal layer showing a protruding cord (e.g. FS/2013/08) and a patient with < 0.5 cm thickness showing an indenting cord (e.g. FS/2013/05).

An additional explanation for the appearances observed beyond hypodermal thickness could relate to the adhesion of the cord to particular tissue layers. In the axilla, an indenting cord could be adherent to skin and underlying layers, showing as a furrow upon abduction. A protruding cord, on the other hand, would be more adherent to the skin, which would be tensed upon abduction producing the classical bowstring appearance in the axilla and is when the cord is most clearly observed. A cord that is merely palpable could then have a stronger connection to the underlying layers or looser connection to the skin, similar to an adherent scar as indicated in Figure 5.3. No clear differences between the presentations could, however, be observed on imaging in the different layers. After physiotherapy, cording became much less noticeable or was not visible at all, possibly because of reduced adhesions keeping the structure in place (Section 5.2.2.1.).

Figure 5.3. *Skin invagination occurs not only in cording, but generally in scar tissue upon movement of the tissue here shown by flexion of the anterior surface of the forearm. Photo courtesy of Jean-Claude Guimberteau, 2015.*

Table 5.4. *Findings of imaging studies in AWS related to fascia and cord visualisation.*

Lead author and year	Sample	Findings	Fascia	Cord visualisation?
Wei, 2013	*n* = 1	Doppler echo showed subcutaneous cords was a vessel	No mention of fascia	Yes
Leduc, 2014	*n* = 15	Hyperechogenic structures at dermal-hypodermal junction on US; MRI showed hyperechogenic infiltration of general tissue	No focal fascial thickening or increased fibrosis found	Yes
O'Toole, 2015	*n* = 5	Striated linear appearance on longitudinal US; honeycomb finding on transverse US	Findings unrelated to fascia	No consistent or reliable indicator of the cord's presence
Koehler, 2014	*n* = 17	No statistical differences occurred between affected and unaffected sides in terms of skin thickness, disorganisation or tissue echodensity	No abnormal fascial structure was identified	No consistent or reproducible identification of the cord

5.2.2.6. Cord visualisation (Results Section 4.7. + Chapter 7)

Cord visualisation is a contentious issue in the AWS literature. In the current study, there was no consistent structure on US that could describe the cord as seen on surface examination. Out of four studies (see Table 5.4) that used imaging to visualise the cord in AWS, only two were confident in finding a structure representing the cord. The reasons for the discrepancy mentioned were because of the cord's origin as a lymphatic vessel (Koehler *et al.*, 2014) which is difficult to visualise on US; the cord's small size (Leduc *et al.*, 2014); lymphedema fluid (O'Toole *et al.*, 2015); or fibrotic and fatty tissue obscuring the cord (Koehler *et al.*, 2014; Leduc *et al.*, 2014). Leduc and colleagues (2014) noted that in an environment that is hyperechogenic such as the hypodermis, a hyperechogenic fibrotic cord would not be noticed.

Although the cord could not be seen directly on the US scans in the current study, its superficial location could aid in understanding the aetiology of the disorder. As mentioned previousl,y according to Stecco (2015) the SAT contains predominantly veins and lymphatic tissues. The cord, being a small structure, possibly corroborates the hypothesis that the cord may be a superficial lymphatic or vein. Generally no vessels or fibrosed vessels could be identified in the current study. Leduc and colleagues (2014) mention that the cord is a very small structure and that their use of a higher frequency US probe (17 MHz vs 12 MHz in the current study), which increases the detail seen in more superficial layers, could explain why they were able to visualise the cord compared to the current and other, similar, studies. Although Wei and colleagues (2013) did not use a higher frequency probe, their use of Doppler imaging indicating flow passing through the cord additionally highlighted a possible vessel as the structure representing the cord. Yanik and colleagues (2003) also showed a very small tubular reduced echoic structure in Mondor's disease but without flow on Doppler US. The radiologist analysing the MRI scans in the current study, however, suggested that the absence of a STIR hyperintensity in the cord indicates neither a patent vessel of either venous or lymphatic origin to be contributing to the cord. It does, however, not exclude a fibrosed vessel or fascial origin to the cord as hypothesised by Salmon and colleagues (2009) and only represented a single patient. More research is required.

In the current study, findings of visualising the cord on MRI included multiple thinner linear fibrotic lines confluencing with subcutaneous adipose and fascial tissue of the upper limb and axilla forming the cord, supported fascial involvement. On MRI, the fibrotic tissue appeared to give a low signal on both T1 and T2, concurring with comparisons of hyperechogenic signals between US and MRI by Fumiere *et al*. (2007). The study by Leduc and colleagues (2014) produced similar findings on MRI. Their study with 15 patients highlighted the cord as being a conglomerate of multiple fibrous SF strands that connected at the skin. The structure appeared next to a lymphocoele, highlighting the cord's possible lymphatic aetiology.

Although the present study showed features mentioned on US and MRI being indicative of fascial inflammation, adhesion formation, fibrosis and densification, most of the authors that used imaging to visualise the cords contents stipulate that there is no involvement of the fascia in their findings (Table 5.4). Koehler and colleagues (2014) mention that no abnormal fascia was noted by the radiologist. O'Toole (2015) mentions the fibrous honeycombed structures they observed were unrelated to fascia. Leduc and colleagues (2014) mention that no focal fascial thickening was observed on US or MRI, nor was there any evidence for scar adhesions or inflammation, although the structure they highlight as the cord consists (confusingly) of fibrous tissue.

The differences in observations (and opinions) may be due to the different definitions of the cord, confusion surrounding what fascia actually is and its involvement in the healing response. Given the cord's adhesive, puckering and tight appearance on surface anatomy, the current study was interested in the fibrotic nature of the cord, fascial involvement and how the cord related to surrounding structures. US alignment, which had not previously been done, was used to attempt to appreciate the fascial continuity by giving a longitudinal and cross-sectional view of how the fasciae and surrounding anatomy are affected in AWS. Although US was used to visualise the cord's contents from a wider perspective, the present study found that MRI was better at visualising the full structure of the cord as it was better able to give an overview of the fibrotic range of the cord and the structures it affected. US showed indicative features rather than a clear structure, possibly due to fat admixture or oedema as highlighted by echotexture changes. On the other hand, Leduc and colleagues (2014) concluded that US was better able to visualise the cord, based on their definition and ability to observe an actual vessel/structure to determine the cord's original aetiology, rather than observing the wider tissues involved which is the focus of the current study. Furthermore, fibrotic tissue as deposited material in the healing process may not be seen to be related to fascia, possibly explaining the conflicting message by Leduc and colleagues (2014) regarding fascial involvement.

Another reason for the discrepancy in whether the fasciae are involved in the cord or not could be related to the limited knowledge regarding fascial anatomy and the subtle changes that can occur in fascial pathology. The present study utilised US terminology and fascial anatomical literature to identify the different structures on imaging and to describe the differences and changes seen in the fascia. US analysis of the fascia is, however, still in its infancy and many radiologists do not examine the tissue very often, if at all (Langevin & Kawakami, 2012). The radiologists used in the AWS imaging studies may thus not be focussed of fascial pathology and hence may miss or dismiss any changes to the fasciae, which could further explain why the cord or features related to it are not easily recognised on US.

The explanations in the current section support the first and second hypotheses of the present study. In the subsequent sections specific US findings will be described in conjunction with the outcome measures .

5.2.3. Outcome measures of SPADI, ROM and QOL

The present section discusses the patient outcome measures in AWS: pain in general, as measured by SPADI and explained by fascial changes (Section 5.2.3.1), range of movement (ROM) changes with fascial explanations (Section 5.2.3.2), and quality of life (QOL) in the FACT-B (Section 5.2.3.3).

5.2.3.1. Pain in AWS (Results Section 4.3. + Chapter 7)

Pain has been found to be associated with AWS patients in most studies (e.g. Lacombe *et al.*, 2009; Moskovitz *et al.*, 2001; Koehler, 2013; Wei *et al.*, 2013, Kepics, 2007; Johansson *et al.*, 2001). Not all patients, however, present with pain generally which appears to be an enigma in the literature in general post-breast cancer treatment (Shamley *et al.*, 2007). In the current study, two patients did not self-report any pain upon initial questioning. The AWS literature suggests figures ranging from 5.4% of the sample in Bergmann *et al.* (2012) to 24.3% in Fabro *et al.* (2012) in terms of pain presence.

The pain experienced in AWS may be described as localised or spreading. Moskovitz and colleagues (2001) described the pain as arising in the affected axilla and radiating to the scar and up into the arm, predominantly upon movement and was described by most patients in the current study. Other studies report pain in the neck, superior to the clavicle and even spreading to the contralateral breast upon manual manipulation of the affected arm (Fourie & Robb, 2009). The pain could also be from other comorbid conditions. In the present study, patient FS/2013/04 experienced neck pain but was attributed to thoracic kyphosis rather than AWS.

Pain has been measured using different scales. Some studies used a visual analogue scale to identify pain (Wei *et al.*, 2013; Lacomba *et al.*, 2009). To explore which actions affected the patient's functioning and possibly led to pain, the present study utilised the standardised SPADI questionnaire.

5.2.3.1.1. SPADI (Results Section 4.4.3. + 4.4.4. + 4.5.3.)

The present study was the first to use the SPADI as a specialised shoulder pain and disability questionnaire to measure pain and disability. The measure showed patients in the current study presented with moderate-to-high scores before physiotherapy ranging from 22-107 out of 130 upon shoulder movement. Moderate-to-high pain intensity experienced by AWS patients was also reported in several other studies (Wei *et al*., 2013; Lacomba *et al*., 2009; Koehler, 2006).

After physiotherapy, a significant reduction for SPADI Pain ($p = 0.0003$) or a median 54%, SPADI Disability ($p = 0.0055$) or a median 35.8%, and SPADI Total ($p = 0.0008$) or a median 42.7% were observed. Comparing the before and after score ranges showed the biggest minima and maxima shift after physiotherapy for both SPADI components and the total SPADI score. The reductions in pain and disability matched with similar findings in ROM (improvements especially on abduction and flexion) and changes observed on imaging (towards more regular, fluid fasciae). Although no statistical correlation between the other outcome measures was found, a general trend was observed and also corroborated by the literature. Fourie & Robb (2009) reported reduced pain after physiotherapy – although no formal measurement was taken – which corresponded to improved mobility.

Further analysis, separating the two domains of the SPADI, showed the pain score being further reduced in its overall contribution to the total score, indicating that disability was the main contributing factor to the SPADI score after physiotherapy (Disability 63.6% vs Pain 36.4%). Disability domain items 'carrying a heavy object', indicating strength, and 'putting an object on a high shelf' and 'washing back' as well as pain domain items such as 'lying on the involved side', showed highest morbidity as shown by the highest contribution to the total score suggestive of pain induced by stretching the affected arm, which is corroborated by long-term findings by Shamley *et al*. (2007), and with the same items affected statistically in comparison to the larger cohort (Section 4.4.4.). Fascial explanations for ROM disability will be discussed in section 5.2.3.2.

The larger cohort comparison highlights that, in the general pool of breast cancer patients, there may be significant debilitation post-breast cancer treatment regardless of whether cording was present. The findings require further research and attention.

5.2.3.1.2. Fascial explanation for pain

Damaged fasciae may explain the functional and pain difficulties experienced by the patients. As pain appears to arise mostly upon movement in AWS, the tension then placed upon injured tissues might be able to explain the pain activation.

Traction on the skin as a result of skin adhesions and restrictions prevent smooth gliding of the fascial tissues and increase tension on the nociceptors causing pain, which can also lead to mechanical irritation and subsequent pain (Fourie, 2014). Adhesions are present in the present study's patients as visualised on US and MRI before physiotherapy as connections between the dermis, SF, DF and muscle. Reduced adhesions after physiotherapy could explain some of the reduced pain in the current study (Bouffard *et al.*, 2008; Myers, 2012).

An additional explanation for tension causing pain could be as a result of the disruption of the tensional network of the skin. The "relaxed skin tension lines", also called Langer's lines, or the lines of force in which the skin is held taut, have been used to instruct surgery where to cut to obtain the best cosmetic outcome (Crumpler & Ghaudhry, 2001; Borges & Alexander, 1962). When a scar crosses the lines, the tension that is put on the healing wound causes widening of the injury gap with resultant worse inflammation, scar tissue, adhesions and a higher risk for hypertrophic scars (Borges & Alexander, 1962; Fourie, 2014). In our AWS patients, the cord runs perpendicularly to skin tension lines in the axilla, possibly explaining some of the biomechanical limitation in ROM that is observed (Venkateswaran, Levy & Copeland, 2004). The skin tension line explanation with regard to movement restriction and pain is new in the AWS literature and could explain why some patients with different cord locations or appearances may suffer less pain but still experience a reduced ROM.

Tension placed on the fascia may also explain pain arising in AWS patients. Recent literature has shown that the fascia is highly innervated with pain receptors that are activated upon stretching

(Schleip *et al.*, 2006). The nociceptors are embedded within all fascia layers (Stecco, 2015). Damaged fascial tissue which has become adhesive and tense as a result of surgery and neoadjuvant treatments in AWS patients could thus explain some of the pain that the patients in the current study experience when stretching the fascial tissues upon movement (Shamley *et al.*, 2007; Fourie & Robb, 2009). Patients with a more radical surgery, resulting in more injured fascial tissue, furthermore appeared to suffer more pain (Shamley *et al.*, 2012). Physiotherapy has been thought to aid in tissue restoration and remodelling, which may have aided in reduced pain after physiotherapy (Schleip, 2012; Meert, 2013).

Specific pathological changes to the matrix of the fascia after injury have been linked to pain, inflammation and loss of function (Lee & Spicer, 2000; Stecco, 2015; Lee & Spiecer, 2000). Fascial fibrosis was especially noticed as thickening of the superficial fascia on US scans in the current study. Langevin and colleagues (2009) in their study found microinjuries in patients with chronic lower back pain and subsequent US analysis showed an increase of 25% in thoracolumbar fascia thickness and echogenicity. Johansson and colleagues (2001), in addition, mention that fibrotic changes apart from pain also appear to lead to reduced strength and fatigue as also seen in the current study analysing the SPADI results. Improvements in regularity of the fasciae, reduced thickness as well as improved continuity and layering after physiotherapy as seen on US in the current study, could explain some of the reductions in pain and may be the result of tissue modification encouraged by physiotherapy (Schleip, 2012; Meert, 2013).

Stecco (2015) describes that, in fibrotic tissue, muscle spindles are not activated, leading to altered joint ROM and pain. Deising and colleagues (2012) observed that pain receptors in, especially, the deep fascia may become sensitised to altered movement patterns as a result of fibrotic tissue, explaining the development of long-term (muscular) pain found in the current study, with patients presenting years post-treatment with pain. The explanations are also supported by Shamley *et al*., 2007.

Straining of the musculature and shoulder components upon altered shoulder movement as a result of myofascial restrictions, and under-activation of some and over-activation of other compensatory muscles, may also lead to muscular pain (Shamley *et* al., 2012). The axillary fascia has multiple fascial connections to the shoulder girdle, explaining movement alterations upon fascial damage. In the present study, compensatory scapular movement on the affected side showed increased internal rotation and was explained by the physiotherapist to be causing possible internal or external impingement leading to pain. An earlier study by Shamley and colleagues (2007) showed that, in breast cancer-treated patients, over-activation of upper trapezius and rhomboid, which are related to scapular movement and would cause altered shoulder movements, were linked to an increased SPADI score. The authors commented that the omission of the connective tissues in their analysis might be able to explain pain and reduced ROM. Improved movement and functionality of the shoulder as shown in the current study after physiotherapy may thus also have led to improved pain measures due to reduced shoulder strain by removing adhesions and tension.

Altered shoulder movements and resulting postural changes as well as an avoidance of particular actions (highlighted by the impaired movements in the SPADI disability section) may also explain the presence of pain. Lacomba and colleagues (2009) suggested that, in AWS patients, there is myofascial pain resulting from activation of the trigger points in latissimus dorsi, infraspinatus, pectoralis major and pronator teres. Myofascial trigger points are located in the muscles and are areas that can become contracted within the myofascia as a result of poor posture or damage, and that can cause local ischaemia which increases nociceptive signalling (Gautschi, 2012). The chronic inflammatory process prevents the unknotting of the trigger point, leading to a chronic myofascial pain syndrome. In the current study, physiotherapy may have aided in reducing the chronic inflammatory process by myofascial stretching. Stretching, as done in the present study, has been thought to remove inflammatory cytokines from the tissue, reducing the inflammatory response and leading to tissue restoration (Schleip, 2012; Meert, 2013). Gradual guidance of remodelling and releasing the myofasciae could thus have aided in reduced pain post-physiotherapy (Fourie, 2014).

The radiation of pain in our patient sample and the literature (Moskovitz *et al.*, 2001) may be explained by the different nerves that transfer the pain signals. Pain within the superficial fascia appears to follow the dermatomal distribution whereas pain arising from deeper fascia follows motor nerves, due to the deep fascia's myofascial continuity (Stecco, 2015). The idea of myofascial expansions from one muscle to another clarifies how different muscles involved in the same directional movement or action have anatomical continuity. Stecco (2015) explains that pain may be followed along the lines of force in the expansions, explaining the radiating pattern upon movement, and names the pattern a "fasciatome". The fasciatome can explain the resulting radiation of painful stimuli or distal parasthesia away from the primary insult over the arm upon particular movements. Stretching, as practised by the physiotherapist in the current study, is suggested to encourage remodelling of collagen in damaged tissue and may also aid in pain relief by releasing receptors which are activated by being confined in a fibrotic tissue and "re-educating" them (Schleip, 2003; Myers & Frederick, 2012; Bouffard et al., 2008).

The abovementioned explanations support the first and second hypotheses of the present study.

5.2.3.2. **ROM** (Results Section 4.4.3. + 4.5.)

Range of movement (ROM) restriction occurs in a large number of patients that resent with axillary cords. All patients in the current study reported reduced shoulder ROM from their baseline. The literature reports a prevalence of 11.4% to 100% of patients having reduced ROM (see, for example, Moskovitz et al., 2001; Tilley, Thomas-MacLean & Kwan, 2009; Rashtak et al., 2012; Davies & Logan, 2010; Johansson et al., 2001).

The literature presents mostly data on abduction and flexion, even though the present study recorded extension, internal and external rotation as well for a better perspective on shoulder disability. Comparing the active shoulder movements between the current study and the literature showed concurrence in abduction and flexion: 37-132° versus 111-139° for flexion and 65-139° versus 90-132° for abduction (Lattanzi, Zimmerman & Marshall, 2012; Koehler, 2013; Wyrick, Waltke & Ng, 2006). The minima of the ranges appeared lower in the present study, indicating that some patients in the current sample may be affected worse than others.

To determine which are the worst affected movements, the ROM values were compared between affected and unaffected arms before and after physiotherapy, which ROM increased the most after physiotherapy using percentage improvement, as well as which movements showed a statistically significant difference on the affected arm after physiotherapy. From the case studies, one can observe that, after physiotherapy, the difference between affected and unaffected arms became smaller, indicating that the ROM values were closer to their baseline than before. Although all movements improved, abduction and flexion showed a statistically significant difference, showing to be the worst affected movements which is supported by the literature (amongst others, Lattanzi, Zimmerman & Marshall, 2012; Koehler, 2013; Wyrick, Waltke & Ng, 2006). Abduction increased with 48.9% ($p = 0.0078$) and flexion showed a 28.3% ($p = 0.0062$) improvement. The changes were further supported by a comparison of the ROM values in the study (see Table 4.4) to the normal ROM values in Table 5.5.

The evaluation showed predominantly the ranges of pre-physiotherapy abduction and flexion to be below normal. After physiotherapy, all ROM values fall in the normal range.

Table 5.5. Linking shoulder ROM, muscles responsible for the action and SPADI items.

Shoulder ROM and SPADI

		Normal ROM women (°) (Barnes *et al.*, 2001)		
Action	**Musculature**	**Dominant**	**Non-dominant**	**SPADI items***
Abduction	Supraspinatus Deltoid	187.6 ± 16.1	188.6 ± 15.4	Reaching high Touching back of neck Washing hair Putting on vest Placing an object on a high shelf#
Extension	Latissimus dorsi Posterior fibers Of deltoid Teres major	67.3 ± 8.7	68.7 ± 9.3	Buttoning up shirt Taking something from back pocket
Flexion	Coracobrachialis Biceps brachii Pectoralis major	176.7 ± 5.5	176.2 ± 5.9	Reaching high Buttoning up shirt Putting on pants Placing an object on a high shelf#
External rotation	Deltoid Infraspinatus Teres minor	104.9 ± 12.0	97.3 ± 11.3	Touching back of neck Washing hair Putting on vest Taking something from back pocket
Internal rotation	Deltoid Subscapularis Teres major Latissimus dorsi Pectoralis major	47.5 ± 11.2	54.5 ± 11.3	Lying on the involved side/ Reaching high Pushing with the involved side Washing back Buttoning up shirt Putting on pants
Protraction	Serratus anterior			Putting on pants

* Both pain and disability items have been included to give a more complete picture of the involvement of the musculature
\# The item as well as item 'carrying a heavy object' involve muscle strength as well
/ The item also involves tenderness of the involved area
The items in red indicate the action that significantly improved after physiotherapy, muscles that were found to be directly affected on MRI and the SPADI items with highest scores.

Interestingly, on the unaffected side, abduction improved with a median 31% and external rotation with a median 21%. Other changes showed a very limited or a slight negative trend, but were within normal ROM (Table 5.5). Although there were no statistically significant changes, the trends highlighted possible changes occurring on the unaffected side as well, not previously discussed in the literature. Fourie & Robb (2009), for example, found that the opposite side was not affected.

To explain the differences seen before and after physiotherapy and to link the movements with findings on imaging and SPADI, the theory around fascia will be described.

5.2.3.2.1. Fascial explanation for limited ROM

Although Hase and colleagues (2006) reported no association between pain and RM upon improvement after physiotherapy, the current study showed a clear trend with significant improvement on both SPADI and ROM measures, even though a correlation between specific movements could not be obtained. Table 5.5 highlights the relationship between the muscles and their actions related to the different measures on the SPADI questionnaire. The movements in red highlight the actions that were significantly improved on the affected arm, the muscles which were shown on MRI to be connected to the fibrous cord mechanically linking the structures, and the items of SPADI that were found to be the most affected, highlighting a biomechanical relationship. As the MRI scans could not visualise the whole structure, and that the scans are from a single patient, limits the full extent of the descriptive correlation.

A physical relationship to the muscles could explain the ROM limitations as found in the present study. Considering that the axilla is a functional assembly point of many different structures and independent movers that are all required to work synchronously, independently but also in a particular glenohumeral rhythm for proper functioning (Shamley *et al.*, 2007), any physical limitations within the area could affect the ROM deficits.

Adhesions between different tissues such as muscles, subcutis and axillary skin as a result of damage to the fat and loose connective tissue in the axilla have been suggested to be a cause of the mechanical limitation (Fourie & Robb, 2009) as visualised in the present study on MRI and US by linear fibrous connecting strands. O'Toole and colleagues (2015) also showed linear, continuous structures which extended into the biceps brachii muscle on US, supporting the idea.

The development of the adhesions was discussed by Lauridsen and colleagues (2005). In a mastectomy patient, where the deep facia of the pectoralis major is removed, they suggest that a strong adhesion forms directly between muscle and skin, inhibiting a smooth gliding movement that allows for motions of abduction, flexion and external rotation, as observed in the current study. In axillary surgery and clearance, the pathological connection forms as a result of the removal of all fibrofatty tissue between the lateral side of pectoralis major and minor and muscles that line the chest wall and axilla and axillary skin (Lauridsen, Christiansen & Hessov, 2005). The adhesions may then be further reinforced by adjuvant treatments, resulting in tougher adherences (Lauridsen, Christiansen & Hessov, 2005). The adhesions as a direct connection could explain the puckered appearance, the tightened feeling with which the patients presented, and the reduced active ROM as well as the tension that is put on the muscle via the adhesions to its deep fascia and muscle fascicles, preventing it from moving – and is visualised as difficult and sluggish movement on the dynamic US videos. Improved ROM after physiotherapy could thus be explained by the breaking of these adhesions as a result of tissue stretching (Bouffard *et al.*, 2008; Myers, 2012).

The stiffness and slow motion could also be the result of the hypodermis, the ECM of the deep fascia and the hyaluronan becoming more rigid in texture due to the densifying response increasing the viscosity of fascial layers as described by Stecco (2015) and causing friction between tissue plains with reduced gliding potential on the dynamic scans. Langevin and colleagues (2011) describe similar results with decreased trunk range of motion and functional ability as a result of reduced gliding in lower back pain patients, with statistically significant reduced shear between the layers. In patients with myofascial neck pain, sternocleidomastoid and scalene fasciae showed a significant increase in the thickness and density correlating to limited neck ROM and pain (Stecco et al., 2014). The latter study also showed reduced fascial thickness with significant restoration of the ROM and reduction in pain after physiotherapy, also demonstrated in the current study. The findings could be explained by the remodelling stimulated and guided by physiotherapy (Fourie, 2014).

Local adhesions can affect tissues at a distance, further contributing to movement limitation, as a result of myofascial continuity (Gautschi, 2012) and highlighted by the concept of biotensegrity (Schleip, 2012). Due to the fascial continuity between the deep fascia of the muscles of the arm and the pectoralis major fascia, which is continuous with the brachial fascia in multiple ways and connects to the axillary fascia which connects to the fascia of the back (Stecco, 2015), any damage to the network can disrupt independent muscular movement along the chain. Biotensegrity may thus explain why the unaffected arm also changed post-physiotherapy as was shown in the percentage improvement after physiotherapy seen in abduction particularly (Figure 4.2). Shamley and colleagues (2012) found a similar phenomenon in their EMG study, showing that there is bilateral morbidity in the shoulder after breast cancer treatment due to reduced muscle activation. The phenomenon was suggested to be as a result of systemic effects of breast cancer treatments but could also be explained by the disruption of the myofascial proprioceptive feedback system as highlighted by Stecco (2009a) in conjunction with the biotensegrity model. Reduced tightness and adhesions after physiotherapy could thus partly explain the improvements seen on both affected as well as unaffected arms.

Another factor to consider, in order to explain movement limitation, is the fibrosis that was visualised within the muscles, as focal fascial thickening of the fascia and as general dense echotexture on the US scans. Table 5.6 highlights the anatomical areas where radiotherapy treatment of the patients took place. The areas overlap with the area of US examination and hence the changes seen can have been as a result of radiotherapy on the muscles caught in the radiation field. Although skeletal muscle is usually radio-resistant, therapeutic doses can affect the muscle and can affect the connective and vascular tissues, explaining the inflammatory and fibrotic response seen in and around the muscular tissue (Jurdana, 2008). Improvements in tissue healing by increased perfusion via deep friction and removing inflammatory cytokines from the tissue may explain the improvements seen in muscles on imaging and improved ROM after physiotherapy (Van den Berg, 2010; Schleip, 2012; Meert, 2013).

Table 5.6. *The anatomical locations of the area of treatment for radiotherapy for the different patients.*

Radiotherapy area	
Participant #	**Anatomical area of treatment**
FS/2013/02	Medial axilla, chest wall
FS/2013/03	Medial axilla, chest wall, supraclavicular triangle / Superior half axilla, supraclavicular triangle
FS/2013/04	Medial axilla, chest wall, supraclavicular triangle
FS/2013/06	Medial axilla, chest wall, supraclavicular triangle / Superior half axilla
FS/2013/07	Medial axilla, chest wall, supraclavicular triangle
FS/2013/09	Medial axilla, chest wall, supraclavicular triangle
FS/2013/10	Medial axilla, chest wall, supraclavicular triangle / Superior half axilla
FS/2013/11	Medial axilla, chest wall

Lastly, behavioural factors affecting the fasciae can also explain movement limitations as found in the current study. Women after breast cancer treatment often present with a protective posture with their arm and shoulder to prevent movement and pain (Shamley *et al.*, 2007; Fourie, 2014). The abnormal posture may, however, lead to altered scapulothoracic movement and brings problems of impingement within the coracoacromial arch and reduced joint stability with subsequent inflammation of the tendons and capsules involved (Shamley *et al.*, 2007; Stecco, 2015). Altered posture may also result in the shoulder muscles and fasciae to tense up in an unnatural position and can lead to movement imbalances (Shamley et al., 2007; Fourie, 2014; Stecco et al., 2014). Muscle weakness and shortening were also found by Shamley and colleagues (2007) and could also contribute to altered scapulothoracic movement and shoulder movement impairment via myofascial continuity. Reduced tissue tightness and pain, possibly as a result of physiotherapy, and the teaching of how to improve posture during physiotherapy sessions, may explain improvements in ROM as well.

The abovementioned explanations support the first and second hypotheses of the present study.

5.2.3.3. FACT-B and quality of life (Results Section 4.4.3.2. + 4.4.4. + 4.5.4.)

The FACT-B questionnaire, which is specifically aimed at patients with breast cancer, has been used in several studies to identify the impact of treatments and interventions on quality of life, or QOL (Davies, Gibbons, Mackintosh & Fitzpatrick, 2009). In the present study it was used to observe whether the changes that occurred after physiotherapy with respect to cording, pain and disability had an impact on the patient's quality of life. No other study looking into AWS utilised the FACT-B questionnaire or rigorously evaluated QOL in the literature (Yeung, McPhail & Kuys, 2015).

In the current study, the median score after physiotherapy showed no statistically significantly difference and was very similar descriptively. Analysing the scores separately did show improvements with a range from 3.3-12.8% with an exception of patient FS/2013/08 who had a reduction of -16.8%. The worsened score in the patient could be due to her comorbid condition of fibromyalgia and slipped disc in her back, and her inability to actively do the exercises to maintain the improvements as explained by the physiotherapist.

As QOL is very dependent on functioning (Fourie, 2014), the improvement in patient's quality of life in the present study could be explained by the corresponding improvements on both ROM and SPADI score. Although there appeared to be a larger difference after physiotherapy that was statistically significant for both SPADI and ROM, the discrepancy in FACT-B score may be explained by FACT-B measuring not only functional scores, but also other domains that may not be changing in the patient's life, reducing the overall effect of the physiotherapy. Further analysis indeed did not show any clear differences between the different contributions of each different domain to the total score.

When comparing the FACT-B scores to other research findings in the local context, the results were consistent with the bigger breast cancer patient cohort as evidenced by statistical analysis, indicating the QOL measure was similar in patients after breast cancer treatment. As FACT-B is a general measure for breast cancer patient's QOL, that it is representative of a larger cohort indicates that dysfunction in AWS patients measured in the FACT-B in the current study may not be significantly different from general functional deficits after breast cancer treatment in the bigger population, which implies substantial morbidity to be present generally and needs addressing in a larger cohort as previously discussed. The dysfunctions as a result of general breast cancer treatment may be understood by the fascial explanations described in the respective pain and ROM sections above (Section 5.2.3.1. + 5.2.3.2.).

5.3. **Physiotherapy** (Chapter 7 **+** Appendix G + J)

The current study adds to the existing evidence that physiotherapy is useful in aiding symptom resolution and improvement, as all patients who received physiotherapy showed improvement after the treatment in our study and three patients experienced full relief of all self-reported symptoms – supporting the second hypothesis of the present study. The extent of the improvement, however, was dependent on person-specific factors including (neo)adjuvant treatments, lifestyle changes and adherence to homework exercises and was difficult to quantify as attempted using a ranking system (see Appendix J).

Although physiotherapy was successfully utilised in a number of case and small group studies, there appears to be a limit to its ability to restore the patient to pre-operation levels of functioning. Besides that damaged tissue does not fully regain its original structure and function (Guimberteau & Armstrong, 2015), longstanding chronic tight scars as evidenced in some patients may not regain their functioning at all, even with physiotherapy, and being so fixed that surgery is the only option to release the tissues (Fourie, 2014), explaining retention of the cords in at least two of the patients post-physiotherapy who had surgery longer than a year before physiotherapy.

In the present study, the main technique used by the physiotherapist was myofascial release, stretching and scar tissue massage to release the cord, to reduce tightening and to improve ROM. On US afterwards, these patients presented decreased adhesions, reduced thickening and increased multilinearity of the superficial fasciae. Myofascial release aims at the different fascial planes and the intersections of muscle and fascia and, once again, highlights the possible fascial contribution to the AWS (Fourie, 2014). Several studies have indicated that myofascial release or similar techniques aid in the resolution of the cord, the relief of pain and improvement in movement (Kepics, 2007; Moreau et al., 2010; Fourie & Robb, 2009; Tilley, Thomas-MacLean & Kwan, 2009). A study by Stecco and colleagues (2014) supports the current study's US findings, i.e. a reduction of fascial thickness to normal levels and a concomitant reduction in pain and disability using a different myofascial technique called Fascial Manipulation that focuses on the deep fasciae. In other studies, myofascial release was shown to improve independent muscle gliding as well as coordination between adjacent myofascial structures (Fourie & Robb, 2009), and was able to remove tissue adherences by stretching adherent layers independently (Bouffard *et al.*, 2008; Myers, 2012).

Although there is very limited research to provide evidence-based recommended treatment (Fourie, 2014), there are some suggestions in the literature as to how physiotherapy aids in improving tissue adherences and fibrotic scar tissues which were seen in the current study and were highlighted in the previous sections. Stretching the fascia has been hypothesised to contribute to functionally changing the fibrotic tissue by encouraging remodelling of collagen to new demands (Myers & Frederick, 2012; Bouffard *et al*., 2008). Furthermore, it has been thought to eliminate water and inflammatory cytokines from the tissue, mitigating the inflammatory response and improve healing (Schleip, 2012; Meert, 2012). Stretching was also suggested to relieve pain by releasing receptors which are activated by being confined to fibrotic tissue and "re-educating" them with skilled stimulation (Schleip, 2003). Deep friction is thought to help in tissue perfusion and subsequent healing (Van den Berg, 2012).

In our study, the majority of the patients improved post-physiotherapy in all domains of pain and disability and reduced functioning on both ROM and SPADI scores. The improvements indicate that myofascial release physiotherapy may be useful in treating the participating patients and relieving their symptomology. However, due to limited availability with the physiotherapist, patients may not have received all the treatments that they would have required for full relief of symptoms. Although the majority of patients who received physiotherapy have improved over time, the current study did not attempt to evaluate physiotherapy and thus the observed changes could possibly be attributed to the normal healing process. Physiotherapy was used in the present study as it was previously found to be beneficial for AWS patients, improving their range of movement and hastening cord resolution. No randomised clinical trials have, however, been done to show the effect of physiotherapy alone on cord resolution. Physiotherapy thus cannot be concluded to be the sole contributor to the improvements. Although some cords may resolve spontaneously as suggested in the literature, a number of patients in the current study presented with cords years after the original surgical treatment. Their improvement with physiotherapy suggests that physiotherapy may aid in improving their outcome. Furthermore, fascial observations and changes on US may be able to guide future treatment. More research including randomised clinical trials is needed to verify the efficacy of myofascial treatment in AWS. Lastly, no research has been done to evaluate whether physiotherapy may aid in preventing AWS from developing e.g. by stretching in the direction of the Langer's lines previously described. More research is needed in this domain as well.

5.4. Limitations of the study

The present study as a pilot and proof-of-concept study to evaluate the involvement of the fascial system in AWS using US was able to present several findings in support of the hypotheses set out in the introductory chapter. There were, however, a number of limiting factors that need to be taken into account and which affected the study's statistical power.

The major limitation of the study was the low sample size of the patients (in keeping with proof-of-concept studies), which affected the ability to perform more powerful statistical analyses and to allow evaluation of different relationships. We were therefore restricted to using non-parametric tests and to describing general trends in order to compare patients. However, comparing SPADI and FACT-B measures to findings in several other studies done in the local context allowed us to make some inferences about a wider cohort.

Although the current study was predominantly descriptive, the few statistical tests used to support the descriptive findings also have limitations. Use was made of the non-parametric Spearman rank correlation and Kruskal-Wallis tests. While the tests are less strict and can be applied to categorical data as was done in the present study, the tests reduce the data to a qualitative form (ranks) which lessens the power of the tests and causes 'exact' information loss (Triola, 2006). Furthermore, the tests are less efficient and require a larger data sample or increased differences (e.g. in the Kruskall-Wallis test) between the comparison groups to be able to reject a null hypothesis (Triola, 2006). The small sample size of the study could then have compromised the tests' abilities.

The Spearman rank correlation tests a monotonic relationship present in the data which was not specifically analysed for the current study's data, affecting the statistical strength of the test (Triola, 2006). To address the multiple comparisons problem, a Bonferroni correction was applied to each section but, given the number of comparisons, the correction could have increased the number of Type II errors occurring, possibly masking any real correlations, and limiting the statistical power of the tests (Peres-Neto, 1999). A larger sample would aid in addressing the abovementioned concerns in the future.

The limited sample size was partly due to time constraints with respect to data collection and the difficulty in finding patients with cording which, as the quintessential symptom of AWS, is often not discovered due it sometimes being a very subtle structure, as exemplified in the current study as well. Also, the result that pain and disability as well as quality of life might not be very different in AWS patients from the general breast cancer-treated patient population could contribute to not easily being able to differentiate AWS patients in the present study. Patients may also not have understood the severity or extent of their symptoms, possibly as they had been downplayed or dismissed by previous health professionals and thus would not mention the symptoms when asked. The current study also lost patients during physiotherapy and for follow-up after physiotherapy due to patient-related variables such as the cost, time and transport to the study settings due to resource constraints (even though the study would reimburse them for transport costs), and patient health factors such as progressive cancer or comorbid disease which could also have affected the studies trends (Harris *et al*., 2011).

Future studies could look into using a FASTRAK protocol, for example, to improve ROM measures (Shamley *et al*., 2012), to use a radiographer to take US quality scans, or use MRI only instead to visualise the involved tissues. Furthermore, we were only able to provide patients with a maximum of six physiotherapy session due to the limited time and availability of the physiotherapist which may have hindered the patients in their recovery potential.

The absence of blinding could have affected and biased the results, especially considering that US is dependent on the skill of the ultrasonographer. The researcher has done US before in an unpublished mini-dissertation showing that US is able to visualise fascia clearly (Paulssen & Shamley, 2012 [unpublished academic mini-dissertation]). The same researcher performed all of the scans to improve consistency and several blinded, independent radiologists observed the ultrasonographs to gain a professional opinion. Although the research took a different approach – observing the connective tissues by US alignment – the radiologists seemed not to focus on the differences and changes in the fascia. The author therefore used his prior knowledge, anatomical knowledge of the area via dissection and from the limited available literature and used terminology by Stecco (2015), to describe the visualised fascia with assistance from the supervisors as anatomists.

To be able to compare the present study's findings with previous studies by Leduc *et al.* (2014) and Koehler (2013), similar US and cord terminology was utilised in the written analysis of the scans. The limited two-dimensional view of the US scans did affect our ability to make suggestions about a three-dimensional structure; the alignment of the longitudinal scans, however, provided a view on fascial continuity which aided in describing the fasciae better. The method could nevertheless be better standardised in future studies. Due to the quality of the US scans, greyscale analysis (as performed by Zaidman and colleagues, 2008) to quantify the fibrotic content, although attempted, could not be executed. For future research, a more experienced radiologist could perform the US scans in three dimensions for both qualitative and quantitative analysis.

The limited time available to obtain information during the observation point appointments, due to patient pain and disability, meant that we were not able to secure all the scans for each patient, which is why certain scans are missing from the patient plates. For example, the patients could not always remain in the ABER position required for US, or achieve the same position as other patients. The discrepancy might have influenced the ability to compare between patients.

Similarly, repeat measurements were not able to be obtained due to the patients experiencing pain and discomfort during the ROM measurements and not being comfortable repeating the same movements, possibly having led to measurement errors as reliability tests could not be performed.

Since the study observed active range of movement as representative of the patient's ability to function, the patient's motivational aspects related to, for example, trying to do what the researcher wants to see, might have changed the patient's ROM. A way to prevent the limitation in a future study is to measure passive ROM where a physiotherapist would take the measures to measure the anatomical limitations of the movements (Clarkson & Gilewich, 1989). Measuring passive ROM could also aid in determining the pathological barrier, where there is a premature end to the passive range of movement (Clarkson & Gilewich, 1989). The restriction indicates an impairment in the soft tissue structures which affects the quality of movement between the tissues.

Lastly, the present study focused on the adhesions being the result of the fibrotic changes occurring after invasive treatments. However, (remaining) malignant cells could also possibly contribute to increased TGF-B production, increased fibrosis and possibly tethered tissues, but these were not considered in the present study. To avoid complications of tumour seeding and spread with physiotherapy, also highlighted in the literature (Langevin *et al*., 2016), future research should consider the possibility in the differential diagnosis of the tethering tissues. More research is needed to look into the contribution of malignant tissues to adhesions and axillary web syndrome in general.

Chapter 6: Conclusions

The current observational, pilot, proof-of-concept study explored the relationship between outcome measures relating to the symptomology of patients with axillary web syndrome (AWS) and clinical and imaging data to elucidate the involvement of the fascial web and its contribution to the symptom complex presented by AWS patients. The study used a case-series design with *n* = 11 patients and addressed two different hypotheses: (1) altered fascia plays a role in the restriction of upper limb movement, the perpetuation of pain and the fibrosis and formation of the cord in AWS; and (2) changes on US images of the cord, fascia and surrounding structures will be evident when the cord resolves or symptoms improve.

To address the first hypothesis, the role of risk factors found in the AWS literature with findings in the present sample and in relation to the facial literature were explored. A younger age as a risk factor for AWS showed similar findings in the current study and was explained by a reduced healing response in the older patients. Increased invasive treatment could be explained to lead to worsened cording using fascial fibrosis, and cord resolution could be explained using the timing of the wound healing cascade but could be complicated by factors such as movement too soon after injury, and abnormal posture. Due to the small sample size, only limited statistical analyses could be performed between different variables, reducing generalisability. The limited statistical power led to uncertainty regarding the contribution of certain factors such as the involvement of (neo)adjuvant treatments in AWS. There is a plausibility, however, that the treatments may be involved in the syndrome as they have been found to be implicated in fibrosis in the literature. Future studies should aim to include larger patient samples to improve their generalisability to the larger cohort.

Other risk factors in the AWS literature appear to contradict the present study's findings. For example, the suggestion that the symptom complex was self-limiting and would disappear within three months post-surgery was shown to be invalid in the current sample as there were women who had experienced relevant symptoms for multiple years. The number of nodes as a measure of extent of invasive treatment may not be a good measure due to the dependency on correct evaluation by the pathologist. Furthermore, the relationship between lower BMI and cording, as found in the literature, may possibly be skewed due to the difficulty of observing the cord in people with increased BMI in the current study. The definition of what the cord is also made comparisons difficult, as some studies considered the cord to be just its original fibrosed vasculature structure, rather than the full fibrotic extent which was regarded as being the cord in the present study. The difference in cord definition also affected measures of cord length which may thus not be a good indication of the full extent of the affected tissue.

Anatomical evidence to answer the first hypothesis was attempted to be provided with imaging. Ultrasonography (US) was utilised as a means to determine any visual fascial abnormalities comparing affected and unaffected arms and descriptively relating the information to the outcome measures of range of movement (ROM), pain and disability as represented by the SPADI questionnaire, and quality of life scores to show how the syndrome affected the patients' daily lives using the FACT-B questionnaire and comparing findings to MRI scans of a single patient.

Ultrasonography, as a cost-effective modality, was found to give a good continuous and dynamic view of the fasciae, their structure and biomechanical functioning, especially using aligned scans. Findings on US scans in n = 11 AWS patients before physiotherapy demonstrated reduced continuity, increased thickening of the longitudinal superficial fasciae bands, decreased gliding potential and increased adherence of fascial layers to each other and the skin. The findings were explained by appreciating the activated and prolonged wound-healing cascade due to invasive and continuous treatment, possible behavioural and movement changes and the role inflammatory cytokines such as TGF-B play in stimulating fibroblasts to produce collagen which may induce subsequent fibrosis and fascial densification.

The US findings corresponded to the surface anatomy in terms of skin puckering, cord appearance and the reduced measures of ROM, and increased pain and disability. The symptoms could be explained theoretically by consulting the fascial literature. Increased adhesions between surfaces, a thick adhesive cord and reduced gliding between muscles as visualised on dynamic US may explain the ROM and disability measures before physiotherapy. Pain could be explained by the development of myofascial trigger points due to local injury and fascial thickening, restrictions and adhesions causing increased traction on the fascia as a result of biomechanical limitations causing nociceptor activation. Quality of life measures did not appear to change very much after treatment, indicating that it might not be a sensitive enough measure in the current cohort of patients, or other factors such as socioeconomic status may be at play.

In the present study, US imaging was unable to visualise the vessel origin leading to the cord, which corroborates most of the studies that have attempted to image the cord. MRI scans, on the contrary, may be a better alternative to US imaging as, in the current study, MRI was clear in being able to show a fibrous band that connected to many different tissues, but MR might not be able to provide enough detail regarding fascial continuity. Future studies could consider using a three-dimensional US to evaluate the fascia from a multidirectional view, but for clinical observation and treatment of AWS, US may be sufficient. In line of the findings discussed regarding the risk factors and imaging, hypothesis (1) was supported.

To address hypothesis (2), we compared changes on US within the fasciae after physiotherapy that focused on treating the myofasciae with aforementioned outcome measures.

Physiotherapy treatment using the myofascial release technique, in particular, appeared to aid in improving the patients' ROM and pain to better states than before. In addition, the majority of patients in the current study resolved their cords or had their cord length much reduced. Improvements on ROM, SPADI and cord measures mirrored observed changes in the US scans such as reduced adhesions between tissue planes, increased tissue gliding and tissue restoration which resembled the fasciae seen in the unaffected arm. US may thus be a feasible outcome measure to evaluate fascia and fibrosis and understand the mechanism by which physiotherapy may be effective as well as guide physiotherapy treatment in the future. Hypothesis (2) was thus also accepted.

Overall, irrespective of the limitations, the present study was able to show that fascial disruption and fibrosis are present in the axilla of patients with AWS. It also provided an overview of how the fasciae – and injury to the connective tissues – can aid in explaining the symptomology present in AWS patients before and after physiotherapy, supporting hypothesis (1) and (2). The symptoms of reduced ROM, pain and cording can be descriptively related to the findings as, upon their improvement, fascial changes were also visible on ultrasound. The findings in the present study were corroborated by the fascial literature that connected movement limitations and pain to similar findings. Additionally, by discussing the anatomical and physiological findings in the literature related to the fasciae, the symptoms were able to be explained which had not been done before. The explanations improve the understanding of the syndrome and can aid in developing new ways for future prevention of the development of cording and related morbidity. Furthermore, although the present study did not attempt to validate physiotherapy as a formal treatment for the participating patients, it is important to recognise that physiotherapy treatment probably has aided in their symptom improvement.

Some recommendations can be made regarding the outcomes of the current study. Given the result that our wider cohort FACT-B and SPADI analyses showed a similar morbidity in patients after breast cancer treatment, there is a need for more recognition and treatment of symptoms to be able to prevent long term sequalae. It is important to challenge a dismissive attitude of – and to instruct – medical doctors to know about and recognise AWS, cording and accompanying symptoms after breast cancer treatment, and to be aware that early diagnosis may prevent long term morbidity. Physiotherapists should be up-to-date with current research regarding treatment of symptoms such as in AWS, and what the recommended treatment is. Patients to receive axillary or breast operations should be made aware of AWS-like symptoms as a possible side-effect and be taught homework exercises and lifestyle modifications in accordance with current research to prevent debilitation. Society needs to be made aware that AWS and similar symptoms exist, how they come about and how they affect women which is important so that more resources can be made available for research to prevent and treat the symptoms. Furthermore, societal awareness could inform public policy to include compensatory measures for patients with breast cancer treatment sequalae in terms of employment, due to the debilitating symptoms.

Future research should look into less invasive treatments for breast cancer to cause minimum morbidity. To understand more about AWS and the involvement of fascia in the syndrome, more imaging studies should be done in patients with cording and better definitions of cording should be developed. Furthermore, validation studies looking into the best treatment for AWS should be done to inform treatment and prevent long-term morbidity. Lastly, risk factors for AWS need to be verified so an early warning system for the sequalae of breast cancer as proposed by Shamley and Robb (2015) could be implemented in a local healthcare setting. A warning system would ensure that patients at risk are identified timeously and measures can be taken to minimise their risk of developing symptoms, that affected patients are recognised as soon as possible, and that they can receive the help they need to minimise the effect of the syndrome on their wellbeing in order to improve their quality of life.

REFERENCE LIST

Abu-Hijleh, M., Dharap, A. and Harris, P., 2012, 'Fascia superficialis' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp.19-25, Elsevier Health Sciences.

Abu-Hijleh, M.F., Roshier, A.L., Al-Shboul, Q., Dharap, A.S. and Harris, P.F., 2006, 'The membranous layer of superficial fascia: Evidence for its widespread distribution in the body', *Surgical and Radiologic Anatomy*, 28(6), 606-619.

Barnes, C.J., Van Steyn, S.J. and Fischer, R.A., 2001, 'The effects of age, sex, and shoulder dominance on range of motion of the shoulder', *Journal of Shoulder and Elbow Surgery*, 10(3), 242-246.

Bauerfeind, I., Himsl, I. and Ruehl, I., 2006, 'Mondor's disease after bilateral axillary node biopsy', *Archives of Gynecology and Obstetrics*, 273(6), 374-377.

Bedrossian, C.W., Miller, W.C. and Luna, M.A., 1979, 'Methotrexate-induced diffuse interstitial pulmonary fibrosis', *Southern Medical Journal*, 72(3), 313-318.

Benjamin, M., 2009. 'The fascia of the limbs and back - A review', *Journal of Anatomy*, 214(1), 1 -18.

Bergmann, A., Mendes, V.V., de Almeida Dias, R., e Silva, B.D.A., Ferreira, M.G.D.C.L. and Fabro, E.A.N., 2012, 'Incidence and risk factors for axillary web syndrome after breast cancer surgery', *Breast Cancer Research and Treatment*, 131(3), 987-992.

Borges, A.F. and Alexander, J.E., 1962, 'Relaxed skin tension lines, Z-plasties on scars, and fusiform excision of lesions', *British Journal of Plastic Surgery*, 15, 242-254.

Bouffard, N.A., Cutroneo, K.R., Badger, G.J., White, S.L., Buttolph, T.R., Ehrlich, H.P., Stevens-Tuttle, D. and Langevin, H.M., 2008, 'Tissue stretch decreases soluble TGF-β1 and type 1 procollagen in mouse subcutaneous connective tissue: Evidence from ex vivo and in vivo models', *Journal of Cellular Physiology*, 214(2), 389-395.

Bulstrode, N.W., Mudera, V., McGrouther, D.A., Grobbelaar, A.O. and Cambrey, A.D., 2005, '5-fluorouracil selectively inhibits collagen synthesis', *Plastic and Reconstructive Surgery,* 116(1), 209-221.

Cancer Association of South Africa, *National Cancer Registry,* viewed 10 February 2013, from: <http://www.cansa.org.za/files/2012/05/Cancer_Registry_2004.pdf>.

Chaitow, L. (ed.), 2014, *Fascial Dysfunction: Manual Therapy Approaches*, Handspring publishers: Scotland.

Cheville, A.L. and Tchou, J., 2007, 'Barriers to rehabilitation following surgery for primary breast cancer', *Journal of Surgical Oncology*, 95(5), 409-418.

Chopra, J., Rani, A., Rani, A., Srivastava, A. and Sharma, P., 2011, 'Re-evaluation of superficial fascia of anterior abdominal wall: A computed tomographic study', *Surgical and Radiologic Anatomy*, 33(10), 843-849.

Clarkson, H.M. and Gilewich, G.B., 1989, *Musculoskeletal Assessment - Joint Range of motion and Manual Muscle Strength,* Williams & Wilkins, Baltimore.

Cleveland, M.G., Ajaikumar, B.S. and Reganti, R., 2000, 'Cutaneous fibrosis induced by docetaxel: a case report', *Cancer*, 88(5), 1078-1081.

Cohen, B.H., Davidson, R.J., Senulis, J.A., Saron, C.D. and Weisman, D.R., 1992, 'Muscle tension patterns during auditory attention', *Biological Psychology*, 33(2-3), 133-156.

Conant, E.F., Wilkes, A.N., Mendelson, E.B. and Feig, S.A., 1993, 'Superficial thrombophlebitis of the breast (Mondor's disease): Mammographic findings', *American Journal of Roentgenology*, 160(6), 1201-1203.

Craythorne, E., Benton, E. and Macfarlane, S., 2009, 'Axillary web syndrome or cording, a variant of mondor disease, following axillary surgery', *Archives of Dermatology*, 145(10), 1199-1200.

Davis, G.G., 1913, *Applied Anatomy: The Construction of the Human Body*, Lippincott.

Davies, N., Gibbons, E., Mackintosh, A. and Fitzpatrick, R., 2009, 'A structured review of patient reported outcomes measures (PROMS) for breast cancer - Report to the department of health', *Patient Reported Outcomes Measurement Group*, University of Oxford.

Davies, S. and Logan, K., 2010, '*Cording following breast cancer surgery: A retrospective analysis and discussion of current literature*', Axillary web syndrome, unknown date, viewed 15 March 2013, from: <http://scholar.googleusercontent.com/scholar?q=cache:S416nGtrAjQJ:scholar.google.com/+K +Logan+cording+axillary+web+&hl=nl&as_sdt=0,5>.

Day, J.A., Stecco, C. and Stecco, A., 2009, 'Application of fascial manipulation technique in chronic shoulder pain: anatomical basis and clinical implications', *Journal of Bodywork and Movement Therapies*, 13, 128-135.

Deising, S., Weinkauf, B., Blunk, J., Obreja, O., Schmelz, M. and Rukwied, R., 2012, 'NGF-evoked sensitization of muscle fascia nociceptors in humans', *PAIN*, 153(8), 1673-1679.

Doriot, N. and Wang, X., 2006, 'Effects of age and gender on maximum voluntary range of motion of the upper body joints', *Ergonomics,* 49(3), 269–281.

Dvorak, H.F., 1986, 'Tumors: Wounds that do not heal. Similarities between tumor stroma generation and wound healing', *New England Journal of Medicine*; 315, 1650–1659

Edge, J., 2004, 'Sentinel node biopsy-its application in the management of early breast cancer: health awareness', *Continuing Medical Education: Your South African Journal of Continuing Professional Development,* 22(10), 585-587.

Engeland, C.G. and Gajendrareddy, P.K., 2011, 'Wound healing in the elderly' in M. Katlic (ed.), *Cardiothoracic Surgery in the Elderly*, pp. 259-270, Springer.

Equator, *EQUATOR NETWORK*, 2013, accessed on 15 May 2016, from <http://www.equator-network.org/>

Fabro, E.A.N., Bergmann, A., e Silva, B.D.A., Ribeiro, A.C.P., de Souza Abrahão, K., Ferreira, M.G.D.C.L., de Almeida Dias, R. and Thuler, L.C.S., 2012, 'Post-mastectomy pain syndrome: incidence and risks', *The Breast*, 21(3), 321-325.

Fallowfield, L.J., Leaity, S.K., Howell, A., Benson, S. and Cella, D., 1999, 'Assessment of quality of life in women undergoing hormonal therapy for breast cancer: Validation of an endocrine symptom subscale for the FACT-B', *Breast Cancer Research and Treatment*, 55(2), 187-197.

Fede, C., Albertin, G., Petrelli, L., Sfriso, M.M., Biz, C., De Caro, R. and Stecco, C., 2016, 'Hormone receptor expression in human fascial tissue', *European Journal of Histochemistry*, 60(4), 224-229.

Findley, T.W., 2007*, Fascia Research: Basic Science and Implications for Conventional and Complementary Health Care,* Elsevier/Urban & Fischer.

Findley, T.W., 2012, 'Fascia-related disorder: An introduction' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 187 -189, Elsevier Health Sciences.

Fourie, W.J., 2008, 'Considering wider myofascial involvement as a possible contributor to upper extremity dysfunction following treatment for primary breast cancer', *Journal of Bodywork and Movement Therapies*, 12(4), 349-355.

Fourie, W.J., 2012, 'Surgery and scarring' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 411-421, Elsevier Health Sciences.

Fourie, W.J., 2014, 'Management of scars and adhesions' in: L. Chaitow (ed.), *Fascial Dysfunction: Manual Therapy Approaches*, pp. 229-243, Handspring Publishing.

Fourie, W.J., and Robb, K.A., 2009, 'Physiotherapy management of axillary web syndrome following breast cancer treatment : Discussing the use of soft tissue techniques', *Physiotherapy*, 95, 314–320.

Friberg, D.C., Nagra, S., Dickson, R. and Thomson, I., 2013, 'Axillary Web Syndrome caused by an insect bite and subsequent fungal infection - Case report', *ANZ Journal of Surgery*, 83, 112.

Fumiere, E., Leduc, O., Fourcade, S., Becker, C., Garbar, C., Demeure, R., Wilputte, F., Leduc, A. and Delcour, C., 2007, 'MR imaging, proton MR spectroscopy, ultrasonographic, histologic findings in patients with chronic lymphedema', *Lymphology*, 40(4), 157-162.

Gautshi, R., 2012, ‘Trigger points as fascia-related disorder’ in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 233-245, Elsevier Health Sciences.

Guimberteau, J.C., 2012, ‘The subcutaneous and epitendinous tissue behaviour of the multimicrovacuolar sliding system’ in R. Schleip, T. Findley, L. Chaitow& P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 143-146,Elsevier Health Sciences.

Guimberteau, J.C. and Armstrong, C., 2015, *Architecture of Human Living Fascia: The Extracellular Matrix and Cells Revealed Through Endoscopy,* Handspring Publishing.

Harris, B., Goudge, J., Ataguba, J.E., McIntyre, D., Nxumalo, N., Jikwana, S. and Chersich, M., 2011, ‘Inequities in access to health care in South Africa’, *Journal of Public Health Policy*, 32(1), S102-S123.

Hase, K., Kamisako, M., Fujiwara, T., Tsuji, T. and Liu, M., 2006, ‘The effect of zaltoprofen on physiotherapy for limited shoulder movement in breast cancer patients: A single-blinded before-after trial’, *Archives of Physical Medicine and Rehabilitation*, 87(12), 1618-1622.

Hassett, G., Harnett, P. and Manolios, N., 2001, ‘Scleroderma in association with the use of docetaxel (taxotere) for breast cancer’, *Clinical and Experimental Rheumatology*, 19(2), 197-200.

Huerta, J.P. and García, J.M.A., 2007, ‘Effect of gender, age and anthropometric variables on plantar fascia thickness at different locations in asymptomatic subjects’*, European Journal of Radiology*, 62(3), 449-453.

Huijing, P.A., 2003, ‘Muscular force transmission necessitates a multilevel integrative approach to the analysis of function of skeletal muscle’, *Exercise and Sport Sciences Reviews,* 31(4), 167-175.

Johansson, K., Ingvar, C., Albertsson, M. and Ekdahl, C., 2001, ‘Arm lymphoedema, shoulder mobility and muscle strength after breast cancer treatment? A prospective 2-year study’, *Advances in Physiotherapy*, 3(2), 55-66.

Josenhans, E., 2007, ‘Physiotherapeutic treatment for axillary cord formation following breast cancer surgery’, *Step up Speak out*, unknown date, viewed March 2013, from <www.stepup-speakout.org/elisabethaws.pdf>*.*

Kepics, J., 2007, ‘Treatment of Axillary Web Syndrome: A case report using manual techniques’, *Dr Vodder School® International*, 10 December, viewed January 2013, from <http://www.vodderschool.com/treatment_of_axillary_web_syndrome>.

Kim, J.H., Park, J.W. and Gong, H.S., 2014, ‘Axillary web syndrome after transaxillary robotic thyroidectomy’, *Journal of Robotic Surgery*, 8(3), 281-283.

Kirk, J.E. and Chieffi, M., 1962, 'Variation with age in elasticity of skin and subcutaneous tissue in human individuals', *Journal of Gerontology*, 17(4), 373-380.

Kirkbride, P., Hatton, M., Lorigan, P., Joyce, P. and Fisher, P., 2002, 'Fatal pulmonary fibrosis associated with induction chemotherapy with carboplatin and vinorelbine followed by CHART radiotherapy for locally advanced non-small cell lung cancer', *Clinical Oncology*, 14(5), 361-366.

Koehler, L.A., 2013, 'Axillary Web Syndrome ongoing medical evaluation', Thesis, Minneapolis, University of Minnesota, viewed March 2013, Open Access Theses and Dissertations.

Koehler, L.A., Hunter, D.W., Haddad, T.C., Blaes, A.H., Hirsch, A.T. and Ludewig, P.M., 2014, 'Characterizing axillary web syndrome: ultrasonographic efficacy', *Lymphology*, 47(4), 156-163.

Lacomba, M.T., Del Moral, O.M., Zazo, J.L.C., Sánchez, M.J.Y., Ferrandez, J.C. and Goni, A.Z., 2009, 'Axillary web syndrome after axillary dissection in breast cancer: A prospective study', *Breast Cancer Research and Treatment*, 117(3), 625-630.

Lacomba, M.T., Sánchez, M.J.Y., Goñi, Á.Z., Merino, D.P., del Moral, O.M., Téllez, E.C. and Mogollón, E.M., 2010, 'Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: Randomised, single-blinded, clinical trial', *British Medical Journal*, 340, 1-8.

Lancerotto, L., Stecco, C., Macchi, V., Porzionato, A., Stecco, A. and De Caro, R., 2011, 'Layers of the abdominal wall: anatomical investigation of subcutaneous tissue and superficial fascia', *Surgical and Radiologic Anatomy: SRA*, 33(10), 835-842.

Langevin, H.M. and Kawakami, Y., 2012, 'Imaging: Ultrasound' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp.483 -489, Elsevier Health Sciences.

Langevin, H.M., Fox, J., Koptiuch, C., Badger, G., Greenan-Naumann, A., Bouffard, N. and Henry, S., 2011, 'Reduced thoracolumbar fascia shear strain in human chronic low back pain', *BMC Musculoskeletal Disorders*, 12(203), 1-11.

Langevin, H.M., Keely, P., Mao, J., Hodge, L.M., Schleip, R., Deng, G., Hinz, B., Swartz, M.A., de Valois, B.A., Zick, S. and Findley, T., 2016, 'Connecting (t)issues: How research in fascia biology can impact integrative oncology', *Cancer Research*, 76(21), 6159-6162.

Langevin, H.M., Stevens-Tuttle, D., Fox, J.R., Badger, G.J., Bouffard, N.A., Krag, M.H., Wu. J. and Henry, M.S., 2009, 'Ultrasound evidence of altered lumbar connective tissue structure in human subjects with chronic low back pain', *BMC Musculoskeletal Disorders*, 10, 151-160.

Lattanzi, J.B., Zimmerman, A. and Marshall, L.M., 2012, 'Case report of axillary web syndrome', *Rehabilitation Oncology*, 30(1), 18-21.

Laug, W.E., DeClerck, Y.A. and Jones, P.A., 1983, 'Degradation of the subendothelial matrix by tumor cells', *Cancer Research*, 43(4), 1827-1834.

Lauridsen, M.C., Christiansen, P. and Hessov, I.B., 2005, 'The effect of physiotherapy on shoulder function in patients surgically treated for breast cancer: a randomized study', *Acta Oncologica*, 44(5), 449-457.

Leduc, O., Fumiere, E., Banse, S., Vandervorst, C., Clement, A., Parijs, T., Wilputte, F., Maquerlot, F., Ezquer-Echandia, M., Tinlot, A. and Leduc, A., 2014, 'Identification and description of the axillary web syndrome (AWS) by clinical signs, MRI and US imaging', *Lymphology,* 47(04), 164-176.

Leduc, O., Sichere, M., Moreau, A., Rigolet, J., Tinlot, A., Darc, S., Wilputte, F., Strapart, J., Parijs, T., Clement, A. and Snoeck, T., 2009, 'Axillary Web Syndrome: nature and localization', *Lymphology*, 42(4), 176.

Lee, J.Y. and Spicer, A.P., 2000, 'Hyaluronan: a multifunctional, megaDalton, stealth molecule', *Current Opinion in Cell Biology*, 12(5), 581-586.

Lee, V.W. and Harris, D.C., 2011, 'Adriamycin nephropathy: A model of focal segmental glomerulosclerosis', *Nephrology*, 16(1), 30-38.

Leidenius, M., Leppänen, E., Krogerus, L. and von Smitten, K., 2003, 'Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer', *The American Journal of Surgery*, 185(2), 127-130.

Levin, S.M. and Martin, D.C., 2012, 'Biotensegrity: The mechanics of fascia' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 137-142, Elsevier Health Sciences.

Luomala, T., Pihlman, M., Heiskanen, J. and Stecco, C., 2014, 'Case study: Could ultrasound and elastography visualized densified areas inside the deep fascia?', *Journal of Bodywork and Movement Therapies*, 18(3), 462-468.

Martelli, G., Miceli, R., Daidone, M.G., Vetrella, G., Cerrotta, A.M., Piromalli, D. and Agresti, R., 2011, 'Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: Results after 15 years of follow-up', *Annals of Surgical Oncology*, 18(1), 125-33.

McNally, E.G. and Shetty, S., 2010, 'Plantar fascia: Imaging diagnosis and guided treatment', *Seminars in Musculoskeletal Radiology*, 14(3), 334-343.

McPherson, K., Steel, C. and Dixon, J.M., 2000, 'ABC of breast diseases: Breast cancer - epidemiology, risk factors, and genetics', *British Medical Journal,* 309(6960), 1003 -1006.

Medical Research Council, 2000, 'A framework for development and evaluation of RCTs for complex interventions to improve health, document record instructions contributor data file', viewed 20 April 2013, from:

<http://www.mrc.ac.uk/consumption/idcplg?IdcService=GET_FILE&dID=9025&dDoName=MRC003372&alowInterrupt=1>

Meert, G.F., 2012, 'Fluid dynamics in fascial tissues' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 177, Elsevier Health Sciences.

Moreau, O., Leduc, O., Tinlot, A., Clement, A., Parijs, T., Strappaert, J., Beckers, F., Pastouret, F. and Leduc, A., 2010, 'Axillary web syndrome (AWS): Its features and the physical treatment plan of care', *European Journal of Lymphology and Related Problems*, 21(59), 25.

Moskovitz, A.H., Anderson, B.O., Yeung, R.S., Byrd, D.R., Lawton, T.J. and Moe, R.E., 2001,'Axillary web syndrome after axillary dissection', *The American Journal of Surgery*, 181(5), 434-439.

MSD Latin America, 'Torso Pictogram', viewed 20 April 2013, from: <http://www.msdlatinamerica.com/ebooks/RockwoodGreensFracturesinAdults/sid980598.html>

Myers, T., 2012, 'Anatomy trains and force transmission' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 131-137, Elsevier Health Sciences.

Myers, T. and Frederick, C., 2012, 'Stretching and fascia', in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 433-441, Elsevier Health Sciences.

Oschman, J., 2012, 'Fascia as a body-wide communication system'. in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 103-113, Elsevier Health Sciences.

Ostoros, G., Pretz, A., Fillinger, J., Soltesz, I. and Dome, B., 2006, 'Fatal pulmonary fibrosis induced by paclitaxel: A case report and review of the literature', *International Journal of Gynecological Cancer*, 16(S1), 391-393.

O'Toole, J., Hannon, K., Skolny, M.N. and Swaroop, M.N., 2015, 'The role of sonographic imaging to assess the pathophysiology of cording in patients treated for breast cancer: A pilot study', *Journal of Diagnostic Medical Sonography*, 31(5), 276-281.

O'Toole, J., Miller, C.L., Specht, M.C., Skolny, M.N., Jammallo, L.S., Horick, N., Elliott, K., Niemierko, A. and Taghian, A.G., 2013, 'Cording following treatment for breast cancer', *Breast Cancer Research and Treatment*, 140(1), 105-111.

Ozturk, C., Yaman, A., Yucesoy, C., and Huijing, P., 2012, 'Advanced MRI techniques for in-vivo biomechanical tissue movement analysis', in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 489-497, Elsevier Health Sciences.

Paulssen, K. and Shamley, D., 2012, ‘Fascial changes after breast cancer treatment’, unpublished academic mini-dissertation, University of Cape Town.

Peres-Neto, PR., 1999, ‘How many statistical tests are too many? The problem of conducting multiple ecological inferences revisited’, *Marine Ecology Progress Series*’, 176, 303-206.

Perez, N.E., Siddiqui, F.A., Mutchnick, M.G., Dhar, R., Tobi, M., Ullah, N., Saksouk, F.A., Wheeler, D.E. and Ehrinpreis, M.N., 2007, ‘Ultrasound diagnosis of fatty liver in patients with chronic liver disease: A retrospective observational study’, *Journal of Clinical Gastroenterology*, 41(6), 624-629.

Purslow, P.P., 2010, ‘Muscle fascia and force transmission’, *Journal of Bodywork and Movement Therapies*’, 14(4), 411-417.

Rashtak, S., Gamble, G.L., Gibson, L.E. and Pittelkow, M.R., 2012, ‘From furuncle to axillary web syndrome: Shedding light on histopathology and pathogenesis’, *Dermatology*, 224(2), 110-114.

Reedijk, M., Boerner, S., Ghazarian, D. and McCready, D., 2006, ‘A case of axillary web syndrome with subcutaneous nodules following axillary surgery’, *The Breast*, 15(3), 410-412.

Rothman, K.J., 2008, ‘BMI-related errors in the measurement of obesity’, *International Journal of Obesity*, 32(S3), S56.

Salmon, R.J., Berry, M.G. and Hamelin, J.P., 2009, ‘A novel treatment for postoperative Mondor’s disease: Manual axial distraction’, *The Breast Journal*, 15(4), 381-384.

Schleip, R., 2003, ‘Fascial plasticity - a new neurobiological explanation: Part 1’, *Journal of Bodywork and Movement Therapies*, 7(1), 11-19.

Schleip, R., 2009, ‘Foreword’ in L. Stecco, C. Stecco, J. Day & R. Schleip (eds.), *Fascial Manipulation: Practical part*, Piccin.

Schleip, R., 2012, ‘Fascia as an organ of communication’ in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 77-81, Elsevier Health Sciences.

Schleip, R., Jäger, H. and Klinger, W., 2012, ‘Fascia is alive: How cells modulate the tonicity and architecture of fascial tissues’ in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 157-165, Elsevier Health Sciences.

Schleip, R., Naylor, I.L., Ursu, D., Melzer, W., Zorn, A., Wilke, H.J., Lehmann-Horn, F. and Klingler, W., 2006, ‘Passive muscle stiffness may be influenced by active contractility of intramuscular connective tissue’, *Medical Hypotheses*, 66, 66–71.

Severeid, K., 2007, ‘Referred to Physical Therapy’, *Rehabilitation*, 25(4), 8-13.

Shahrokni, A., Saif, M.W. and Cornfeld, D., 2007, ‘Gemcitabine-induced liver fibrosis in a patient with pancreatic cancer’, *Journal of the Pancreas*, 8(4), 460-467.

Shamley, D., 2012-2014, unpublished raw data, University of Cape Town.

Shamley, D. and Robb, K.A., 2015, ‘An early warning surveillance programme for detecting upper limb deterioration after treatment for breast cancer: A novel technology supported system’, *BMC Cancer*, 15(1), 635-638.

Shamley, D., Lascurain-Aguirrebeña, I., Oskrochi, R. and Srinaganathan, R., 2012, ‘Shoulder morbidity after treatment for breast cancer is bilateral and greater after mastectomy’, *Acta Oncologica*, 51(8), 1045-1053.

Shamley, D., Srinanaganathan, R., Weatherall, R., Oskrochi, R., Watson, M., Ostlere, S. and Sugden, E., 2007, ‘Changes in shoulder muscle size and activity following treatment for breast cancer’, *Breast Cancer Research and Treatment*, 106(1), 19-27.

Shetty, M.K. and Watson, A.B., 2001, ‘Mondor's disease of the breast: Sonographic and mammographic findings’, *American Journal of Roentgenology*, 177(4), 893-896.

Shultheis, A., Reichwein, F. and Nebelung, W., 2012, ‘Frozen shoulder’ in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 199-207, Elsevier Health Sciences.

StatSoft®, 2013, *STATISTICA 12*, unknown date, viewed 25 May 2013, from <http://www.statsoft.com/products/>.

Stamenkovic, I., 2000, ‘Matrix metalloproteinases in tumor invasion and metastasis’, *Seminars in Cancer Biology*, 10(6), 415-433.

Standring, S. (ed.), 2008, *Gray’s Anatomy*, 40th ed., Churchill Livingstone.

Stecco, C., 2015, *Functional Atlas of the Human Fascial System,* Elsevier Health Sciences.

Stecco, C. and Stecco, A., 2012, ‘Deep fascia of the shoulder and arm’, in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 25-31, Elsevier Health Sciences.

Stecco, A., Macchi, V., Stecco, C., Porzionato, A., Day, J., Delmas, V. and De Caro, R., 2009a, ‘Anatomical study of myofascial continuity in the anterior region of the upper limb’, *Journal of Bodywork and Movement Therapies*, 13(1), 53-62.

Stecco, C., Macchi, V., Porzionato, A., Duparc, F. and De Caro, R., 2011, ‘The fascia: The forgotten structure’, *Italian Journal of Anatomy and Embryology*, 116(3), 127-138.

Stecco, A., Meneghini, A., Stern, R., Stecco, C. and Imamura, I., 2014, ‘Ultrasonography in myofascial neck pain: Randomized clinical trial for diagnosis and follow-up’, *Surgical Radiological Anat*omy, 36(2), 243-253.

Stecco, C., Porzionato, A., Macchi, V., Tiengo, C., Parenti, A., Aldegheri, R., Delmas, V. and De Caro, R., 2006, ‘A histological study of the deep fascia of the upper limb’, *Italian Journal of Anatomy and Embryology*, 111(2), 105-110.

Stecco, L., Stecco, C., Day, J.A. and Schleip, R., 2009b, *Fascial manipulation: Practical part*, Piccin.

Stone, H.B., Coleman, C.N., Anscher, M.S. and McBride, W.H., 2003, ‘Effects of radiation on normal tissue: Consequences and mechanisms’, *The Lancet Oncology*, 4(9), 529-536.

Tilley, A., Thomas-MacLean, R. and Kwan, W., 2009, 'Lymphatic cording or axillary web syndrome after breast cancer surgery', *Canadian Journal of Surgery*, 52(4), E105-E106.

Triola, M.F., 2006, *Elementary Statistics*, 11th ed., Pearson/Addison-Wesley.

Van den Berg, F., 2012, 'Extracellular matrix' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 165-171, Elsevier Health Sciences.

Van der Wal, J., 2012, 'Proprioception' in R. Schleip, T. Findley, L. Chaitow & P. Huijing (eds.), *Fascia: The Tensional Network of the Human Body*, pp. 81-89, Elsevier Health Sciences.

Venkateswaran, B., Levy, O. and Copeland, S., 2004, 'Surgical approaches for instability surgery of the shoulder', *Current Orthopaedics*, 18(2), 85-96.

Wei, P., Zhu, L., Chen, K., Jia, W., Hu, Y. and Su, F., 2013, 'Axillary web syndrome following secondary breast-conserving surgery: A case report', *World Journal of Surgica Oncology*, 11(1), 8, 1-2.

Williams, J.J., Holleman, J.D. and Simel, D.L., 1995, 'Measuring shoulder function with the Shoulder Pain and Disability Index', *The Journal of Rheumatology*, 22(4), 727-732.

Wyrick, S.L., Waltke, L.J. and Ng, A.V., 2006, 'Physical therapy may promote resolution of lymphatic cording in breast cancer survivors', *Rehabilitation Oncology*, 24(1), 29-34.

Yang, G., Im, H.J. and Wang, J.H.C., 2005, 'Repetitive mechanical stretching modulates IL-1β induced COX-2, MMP-1 expression, and PGE 2 production in human patellar tendon fibroblasts', *Gene*, 363, 166-172.

Yanik, B., Conkbayir, I., Öner, Ö. and Hekimoğlu, B., 2003, 'Imaging findings in Mondor's disease', *Journal of Clinical Ultrasound*, 31(2), 103-107.

Yavas, G., Yavas, C., Acar, H., Toy, H., Yuce, D. and Ata, O., 2013, 'Comparison of the effects of aromatase inhibitors and tamoxifen on radiation-induced lung toxicity: Results of an experimental study', *Supportive Care in Cancer*, 21(3), 811-817.

Yeung, W.M., McPhail, S.M. and Kuys, S.S., 2015, 'A systematic review of axillary web syndrome (AWS)', *Journal of Cancer Survivorship*, 9(4), 576-598.

Yu, T.K., Whitman, G.J., Thames, H.D., Buzdar, A.U., Strom, E.A., Perkins, G.H., Schechter, N.R., McNeese, M.D., Kau, S.W., Thomas, E.S. and Hortobagyi, G.N., 2004, 'Clinically relevant pneumonitis after sequential paclitaxel-based chemotherapy and radiotherapy in breast cancer patients', *Journal of the National Cancer Institute*, 96(22), 1676-1681.

Zaidman, C.M., Holland, M.R., Anderson, C.C. and Pestronk, A., 2008, 'Calibrated quantitative ultrasound imaging of skeletal muscle using backscatter analysis', *Muscle & Nerve*, 38(1), 893-898.

Chapter 7: Supplementary Information – Patient Case Studies

7.1. Patient FS/2013/01

Table 7.1. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	48 years	
Side affected	Left and right	
Handedness	Left	
Treatments	**Surgery**	Bilateral mastectomy and left SLND
	Chemotherapy	Gemcitabine (x2) and CEF (x4)
	Radiotherapy	-
	Hormonal therapy	-
No. of days surgery until presentation	70 days	
Self-reported symptoms before	Axillary tightness, pain and reduced range of movement	
Self-reported symptoms after	None	
No. of physiotherapy treatments	5	
Physiotherapy focus	Scar adherence release; myofascial release along chest wall, axilla, upper arm with a greater focus on the left arm; scapular mobilisation; mobilising and stretch homework exercises	

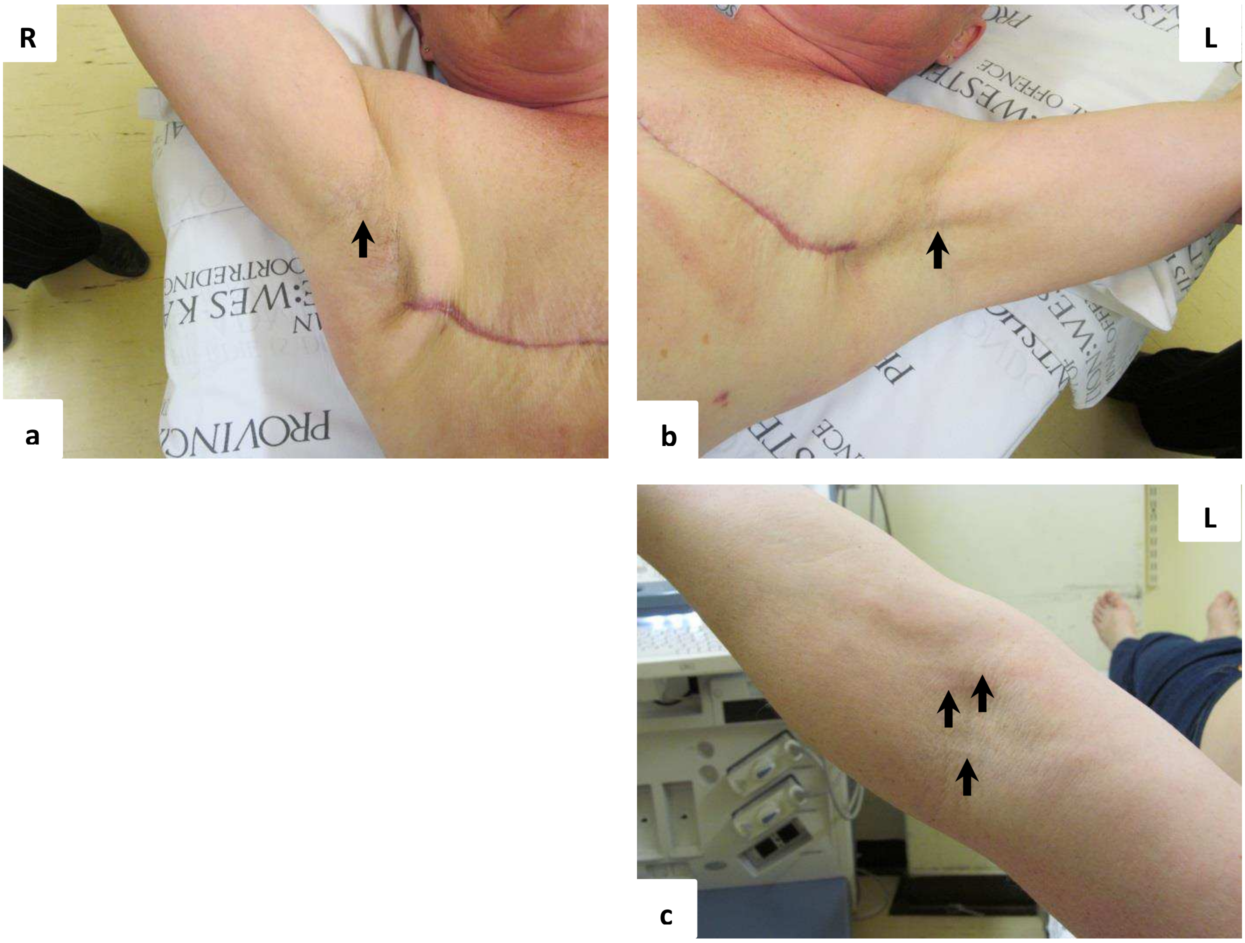


Figure 7.1. *With the arm in the ABER position, showing the cord (arrows) and scar area for patient FS/2013/01 before physiotherapy. The third photograph (c) illustrates the extension of a web of smaller cords (arrows) into the cubital fossa of the elbow on the left arm.*

7.1.1. Patient description

A 48-year-old woman presented 70 days post-surgery with bilateral cording, tightness on the chest wall and in the axilla, limited shoulder movement and pain upon movement (Table 7.1, Figure 7.1).

The patient was treated with a left mastectomy and sentinel lymph node dissection on the left for breast carcinoma and a right prophylactic mastectomy with no axillary surgery on the right side. The patient was being treated with two cycles of gemcitabine and was due to receive four cycles of the CEF regimen which she finished during the course of her physiotherapy treatment. No other adjuvant treatments were prescribed during the study.

The physiotherapist reported more puckering, tightness and impairment on the left side and therefore focused on the left, but treated both arms with myofascial release into the chest wall, axilla and upper arm, the muscles pectoralis major and minor and serratus anterior and posterior, and by mobilisation of shoulder and scapula to improve scapulothoracic movement.

7.1.2. Surface anatomy

Figure 7.1 shows that the cord on the left side is more prominently bulging outwards and seemingly thicker (b) extending branches down towards the cubital fossa (c), whereas the cord on the right is more guitar-string like with the skin being pulled inwards (a). Both appear to lie between coracobrachialis and teres major muscles.

After physiotherapy both cords have resolved (Figure 7.2).

Figure 7.2. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/01 after physiotherapy. L=left, R=right.*

7.1.3. Measurements

At the first measurement cycle, the axillary cords measured 100.43 mm on the left (with a web extending further down) and 100.11 mm on the right which were completely resolved after the five physiotherapy treatments at the second measurement cycle.

The patient's SPADI score mirrored the cord size difference as she reported a higher pain and disability score on the left compared to the right (L: 78 versus R: 70; Table 7.2). With a similar score for lying on the involved side (9/10) bilaterally, reaching high (9 versus to 7) and putting an object on a high shelf (9 versus 6) proved more painful and difficult on the left. The total scores decreased by 88% on the left and by 66% on the right, possibly due to the physiotherapy focus on her left arm. The right showed the highest score for pushing with the involved arm and carrying a heavy object (4/10), both scores being related to muscle strength.

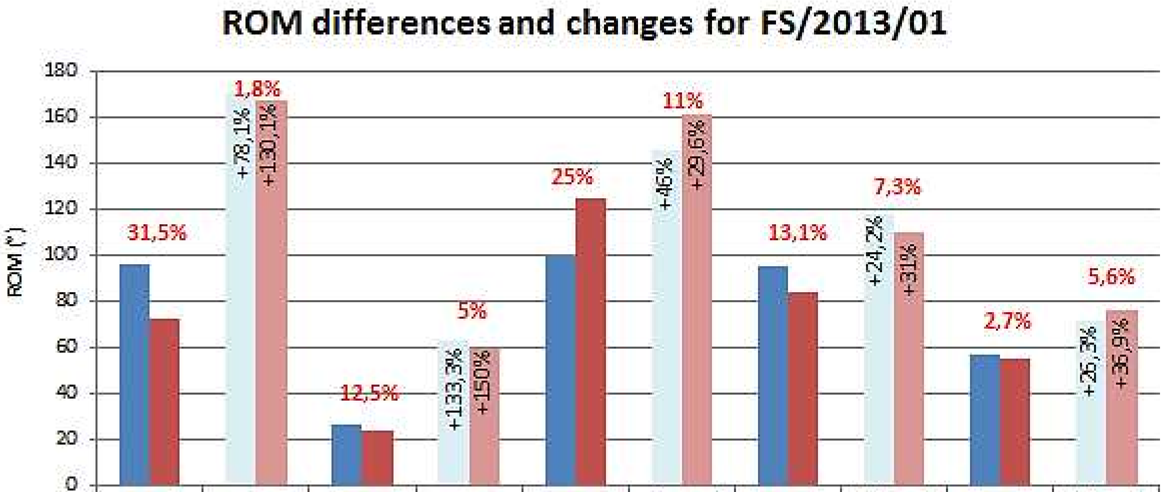
The patient's FACT-B score showed relatively low scores for the physical subsection (10/28), where she scored herself as very much having (4/4) pain, feeling ill and being nauseous, and in the additional concerns subsection (16/36) in which she indicated she was worried about the effect of stress on her illness and she had lots of places in her body where she felt pain. The responses linked to the SPADI with a (±35/50=) 70% pain score. After physiotherapy her overall score improved very little with only a 5% increase to 84.4/144, even though the SPADI decreased and range of movement increased.

Table 7.2. *Percentage change of cord length, SPADI and Fact-B scores after physiotherapy. L=left, R=right.*

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	L: 100.43/ R: 100.11	L/R: 0	**L/R: -100**
SPADI (pain)	L: 39/ R: 35	L: 6/ R: 14	**L: -84.6/R: -60**
SPADI (disability)	L: 39/ R: 35	L: 3/ R: 10	**L: -92.3/R: -71.4**
SPADI (total)	L: 78/ R: 70	L: 9/ R: 24	**L: -88.4/ R: -65.7**
FACT-B (physical)	10	9	**-10**
FACT-B (social)	15,2	23,3	**+53.3**
FACT-B (emotional)	21	21	**0**
FACT-B (functional)	18	18	**0**
FACT-B (additional concerns)	16	13	**-18.8**
FACT-B (total)	80.2	84,3	**+5.1**

The patient's ROM before and after physiotherapy is depicted in Figure 7.3. Comparing the before and after data it can be observed that all the actions improved with more than 25% after physiotherapy. The most improved and thus affected actions are extension on both sides (L: 133.3%/R: 150%) and abduction on the right (130%). Except for internal rotation, the difference between both arms reduced after physiotherapy in all other actions and thus the ROM of both arms became more similar.

Although the cord and SPADI were worse on the left side, it did not necessarily reflect in the range of movement, apart from forward flexion where there was a difference before physiotherapy of 25% compared to the right side. A link with the 20% difference in SPADI scores between left and right after physiotherapy was not clearly observable from the change in ROM values, but perhaps related to her being left-handed.



	Abduction	Abduction after	Extension	Extension after	Forward flexion	Forward flexion after	External rotation	External rotation after	Internal rotation	Internal rotation after
Left	96	171	27	63	100	146	95	118	57	72
Right	73	168	24	60	125	162	84	110	55,5	76

Figure 7.3. *The difference between left and right arms and improvement on range of movements for patient FS/2013/01 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*

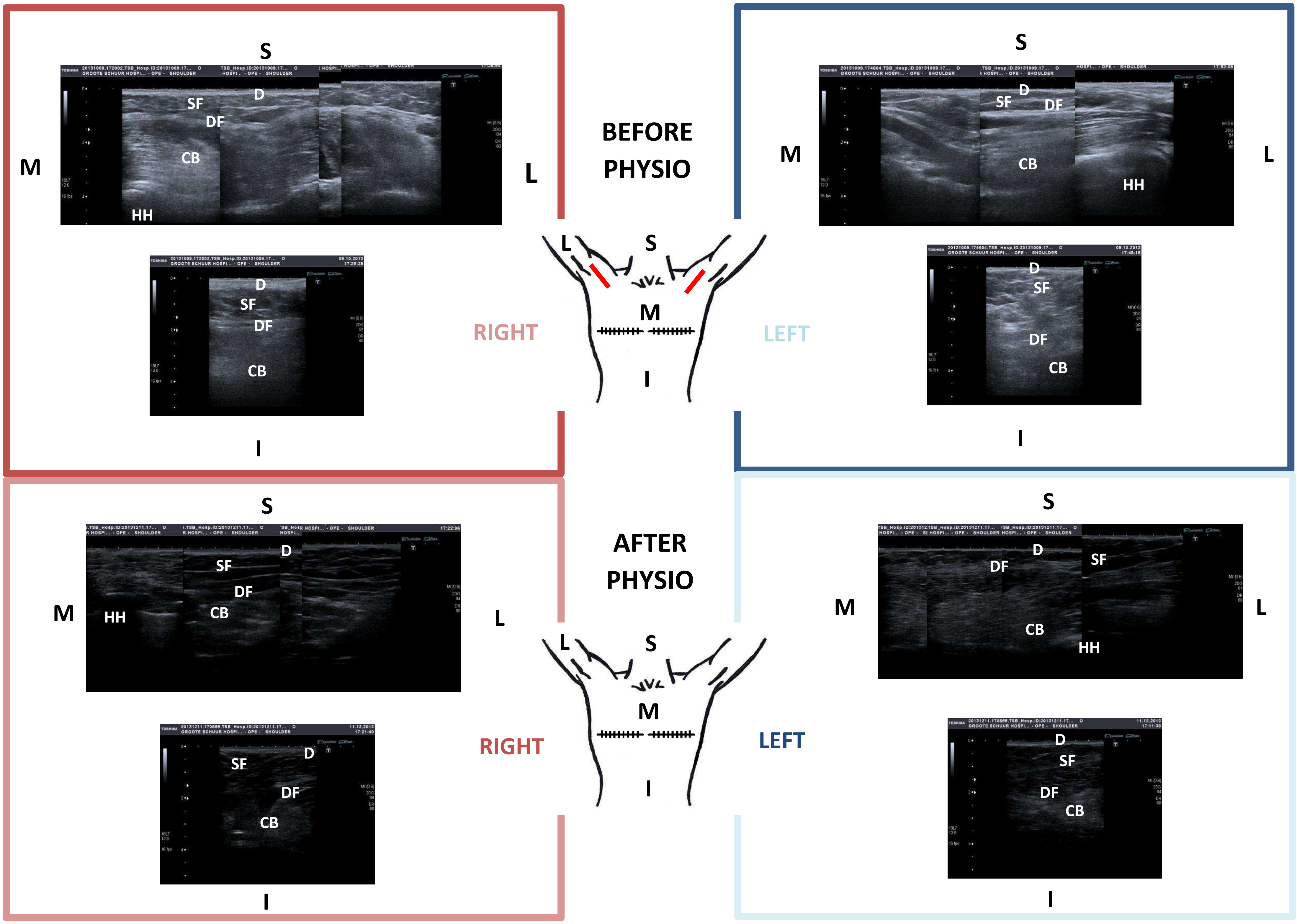

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Plate 7.1.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/01 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.1.4. Ultrasonography Plate 1

7.1.4.1. Static

7.1.4.1.1. Left

A variable layer of between 1-1.5 cm of adipose tissue was visible on the longitudinal ultrasound scans before physiotherapy. The superficial fascia layer (SF) which was closely related to the skin, appeared more thickened and hyperechoic, expecially in the middle and close to the deep fascia (DF), throughout the superficial adipose tissue and irregular, broken strands appeared to originate from it. It had a coarse but dense area of homogeneity in echotexture closer to the skin on the right. The DF showed some continuation with the SF, showed much thickened but appeared ill-defined on the transverse scan. The CB showed slight increased echotexture within it. The transverse scan further showed an irregular heterogeneity with hyperechoic strands in the adipose tissue within which vessels openings were noted.

After physiotherapy, although still slightly thickened there were more defined multiple continuous striae of superficial fascia compared to before physiotherapy on the longitudinal scans or compared to the right side after treatment. On the transverse scan the superficial fascial layer was more continuous than before and was clearly separated from the DF by the deep adipose tissue and its retinacula cutis profundus.

7.1.4.1.2. Right

Comparable to the left, on the pre-physiotherapy longitudinal scans of the right side there was approximately 1 cm of adipose tissue visible at the location of the cord. There was increased echogenicity with thickened, irregular fascial bands in the superficial adipose tissue. It also had a honeycomb appearance. The deep fascia (DF) over the coracobrachialis muscle was hyperechoic and had a width of approximately 0.35 cm. There seemed to be increased homogenous echotexture within the coracobrachialis muscle itself, which was also visible on the transverse scans. On the transverse scan, taken mid-cord, there were fossae for vessels present within the adipose tissue as well as a thickened coracobrachialis fascia.

Post-treatment, the longitudinal scans on the right side showed more regular linear bands of superficial fascia within the hypodermis with a thinner coracobrachialis muscular fascia. There was still some increased echogenicity, but the echogenicity was much decreased after cord resolution and there was little difference in echotexture.

7.1.4.2. Dynamic

On the left one could see tightening of all the fascial layers in conjunction when attempting to move the arm (Video 1.1). More fluid movement and more gliding potential between the deep fascia and the muscle was visible in video 1.2 after physiotherapy.

In Video 1.3 on the right the adipose tissue was observed to be restricted in movement whilst the patient was moving her arm in the ABER position. There also seemed to be very little gliding between the SF, DF and muscle. After physiotherapy, some gliding between the layers seemed to have been restored though the video is unclear (Video 1.4).

7.1.4.3. Links between outcome measures

Although no definite cord structure appeared on the ultrasonographs, there were distinct fascial differences before and after physiotherapy and between left and right sides. A thicker and more dense homogeneous SF on the left side may have correlated to the thicker more invasive axillary cord as observed on surface anatomy, compared to the thinner SF more honeycombed structure on the right with the less obvious cord. There also seemed to be more regularity and more fluid, independent movement with fascial gliding between the separate layers after physiotherapy, more on the left than on the right, on the dynamic videos. The findings corresponded to the reduced pain and disability scores as well as to the much improved ROM and side differences, although both sides showed definite signs of improvement.

7.2. Patient FS/2013/02

Table 7.3. Participant variables describing age, affected side, handedness and treatment details.

Patient details		
Age	38 years	
Side affected	Right	
Handedness	Right	
Treatments	**Surgery**	Right mastectomy + right ANC
	Chemotherapy	CEF (3x) + paclitaxel (4x)
	Radiotherapy	41.6 Gy (3.2 Gy/frac) chest wall + medial axilla; 38.4 Gy (3.2 Gy/frac) supraclavicular area + superior half of axilla
	Hormonal therapy	-
No. of days surgery until presentation	149	
Self-reported symptoms before	Cording and limited range of movement	
Self-reported symptoms after	Cording	
No. of physiotherapy treatments	8	
Physiotherapy focus	Scar tissue massage; myofascial release over chest wall, axilla, upper and forearm; adherent superficial and deep fascia; increased chest wall tightness after RT; homework stretches	

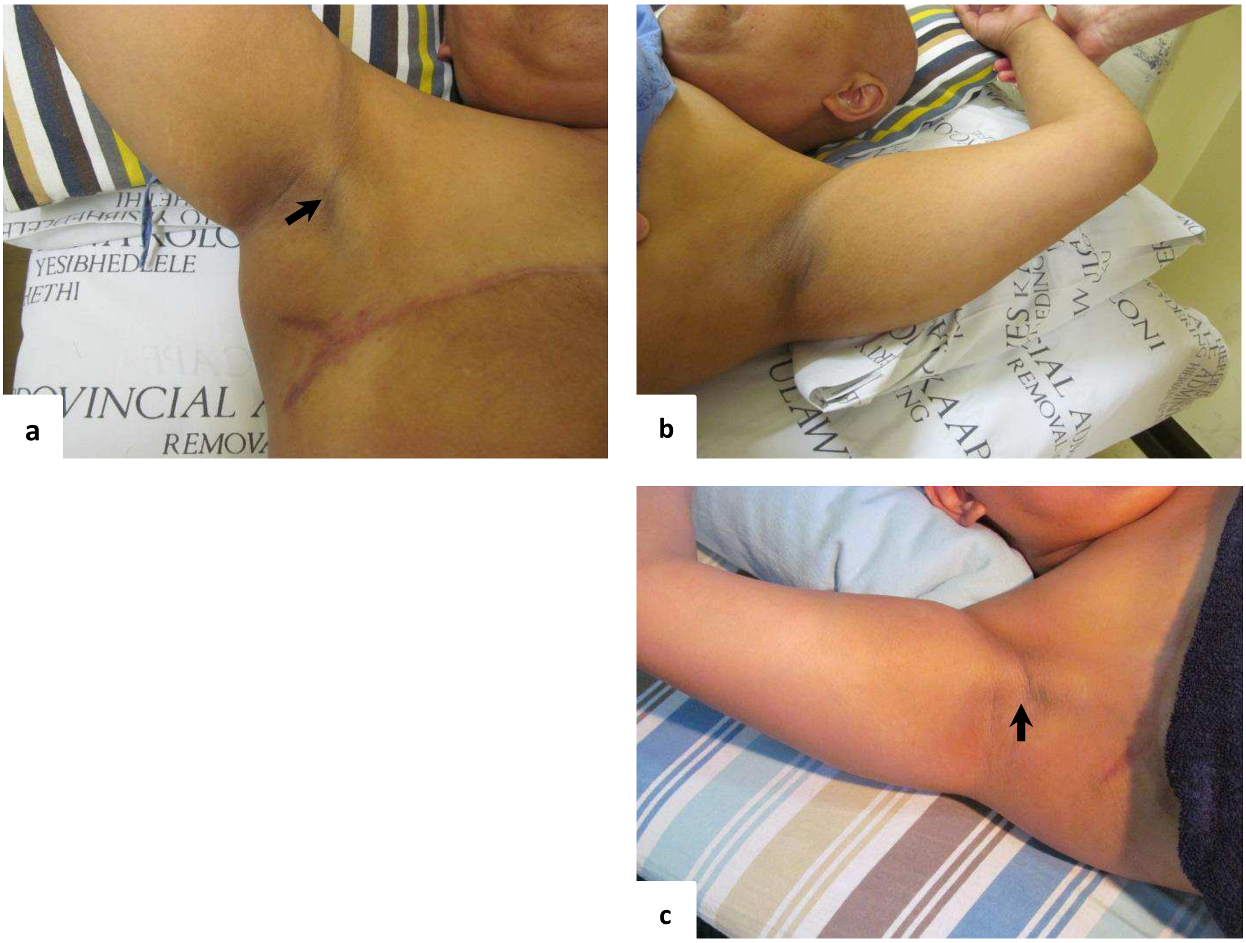

Figure 7.4. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/02 before (a,b) and during physiotherapy before radiotherapy (c). Arrows indicate the cord position. L=left, R=right.*

7.2.1. Patient description

A 38-year-old woman presented 149 days post-surgery with cording in the right axilla, a very adherent scar and reduced shoulder movement that left her unable to continue her work as a nursing aid (Table 7.3, Figure 7.4).

The patient's breast cancer treatment consisted of a right mastectomy with axillary node clearance on the same side. The patient had received her first three CEF chemotherapy courses and continued with four paclitaxel courses and 41.6 Gy radiotherapy to the chest wall (3.2 Gy/frac) and 38.4 Gy to the supraclavicular area (3.2 Gy/frac) during the course of her physiotherapy treatment.

The physiotherapist focused her treatment on the scar area and myofascial release over pectoralis major and minor, coracobrachialis, short head of biceps, serratus anterior, infraspinatus, latissimus dorsi, rhomboid major and minor, levator scapulae and trapezius. The patient's physiotherapy treatment had to be discontinued for a month for the tissues to recuperate before commencing again and the patient's treatment was extended with three more treatments to recover the patient's achieved range of movement and reduce the redeveloped tightness across the chest wall after radiotherapy.

7.2.2. Surface anatomy

Figure 7.4a showed the finger-thick cord on the right side extending from the chest wall over the axillary fossa into the antero-medial aspect of the upper arm and the limitation of the arm. The cord appeared more medially lying between coracobrachialis and teres major muscles and was bulging out in the ABER position. On Figure 7.4c the improvement after four physiotherapy treatments was noted and showed much improved range of motion and a remnant of the cord.

Figure 7.5. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/02 after physiotherapy with the arm in the ABER position. Arrow indicates the cord position. L=left, R=right.*

On Figure 7.5, three physiotherapy treatments after RT, it was noted that the skin looked darkened, the range of movement was reduced and the unresolved cord indented into the axillary fossa.

7.2.3. Measurements

At the first measurement cycle, the cord length was measured to be 98.6 mm. It showed an improvement of 34% after physiotherapy with a cord that subsequently measured 64.5 mm in length (Table 7.4).

Even though the cord did not resolve, a vast improvement in both SPADI pain and disability scores was observed with an overall reduction of 75% to 26 out of 130 for the total SPADI score. Especially items where she scored high before such as 'reaching high' and 'putting an object on a high shelf', 'touching the back of the neck', 'washing her back' and 'putting a pants on' showed marked improvements from generally 10 to 2. The scores correlated with the patient feeling better, more active and feeling that her arm was less tight, as reported by the physiotherapist.

Her Fact-B score improved only slightly with 9.5%, even though her physical and functional scores improved, potentially due to extraneous factors.

Table 7.4 *Percentage change of cord length, SPADI and Fact-B scores after physiotherapy. L=left, R=right.*

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	98.61	64.46	**-34.6**
SPADI (pain)	33	4	**-87.9**
SPADI (disability)	71	22	**-69**
SPADI (total)	104	26	**-75**
FACT-B (physical)	5	12	**+40**
FACT-B (social)	26	20	**-23.1**
FACT-B (emotional)	24	20	**-16.7**
FACT-B (functional)	13	18	**+38.5**
FACT-B (additional concerns)	18	24	**+33.3**
FACT-B (total)	85.7	93.8	**+9.5**

The ROM measurements in Figure 7.6 showed a continued difference between affected and unaffected arms even after physiotherapy, with differences of over 15% for abduction, forward flexion and external rotation. Although abduction improved with approximately 50% for each side, only minor improvements or decreases (of up to 33% in external rotation) were seen on the affected side for other movements. The reduced changes could be due to the remnant cord and retightening of the tissues after radiotherapy even though functionally she felt better as shown by the SPADI score.

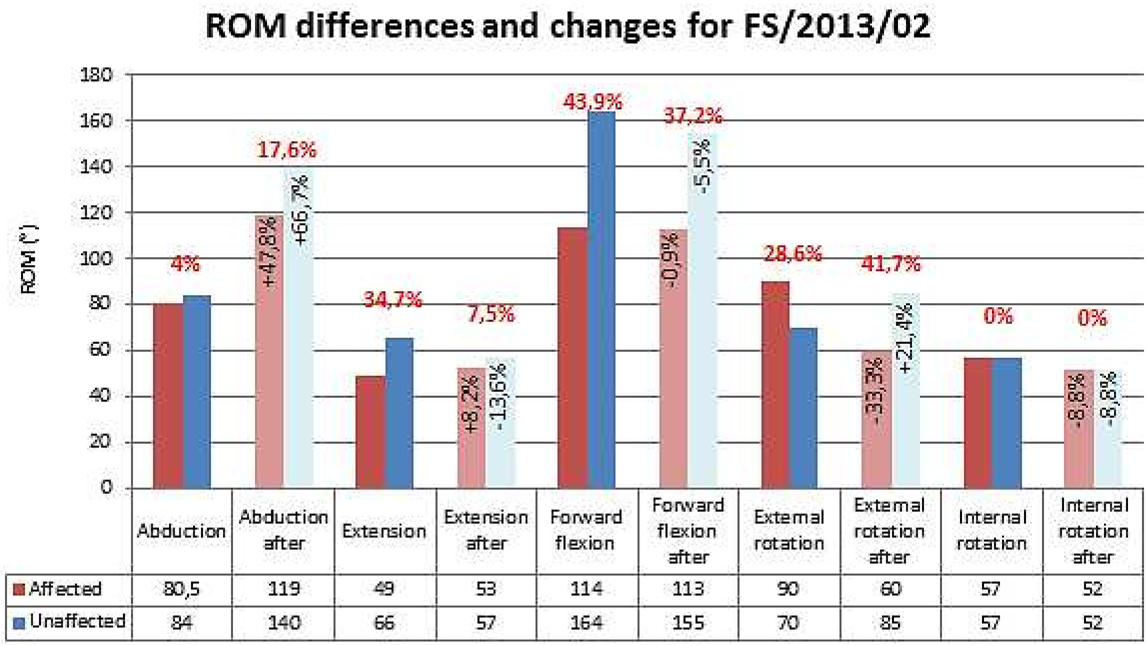

Figure 7.6. *The difference between left and right arms and improvement on range of movements for patient FS/2013/02 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*

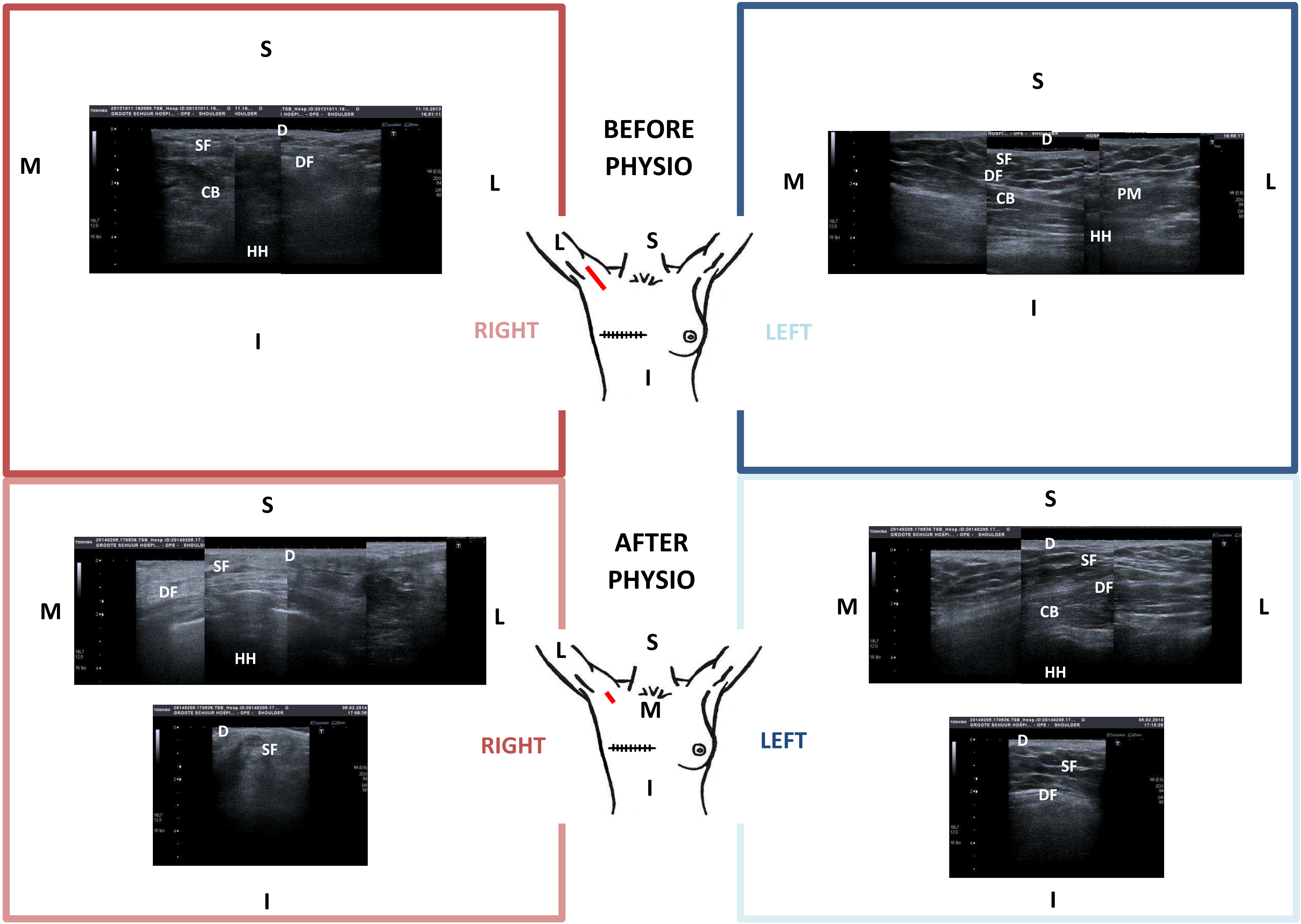
BEFORE
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Plate 7.2.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/02 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, PM=pectoralis major muscle, HH=humeral head.

7.2.4. Ultrasonography Plate 2

7.2.4.1. Static

7.2.4.1.1 Left

On the left side the different compartments were very clearly defined. An adipose tissue layer of approximately 1-2 cm was noted on the longitudinal scans with a superficial fascia that was continuous and consisted of multiple converging layers. It was connected to the dermis and to the deep fascia. The deep fascia lines extended into the coracobrachialis muscle in which we could clearly see the individual muscle fascicles demarcated. There was little difference on the post-physiotherapy scans, showing fascial continuity and vessel lumen in a honeycomb fashion on the transverse scan.

7.2.4.1.2. Right

On the pre-treatment longitudinal scans, a very heterogeneous echotexture throughout the different tissue compartments without clear distinction between them, was observed. The superficial fascia (SF) seemed thickened (±0.5 cm) and consisted of densely packed hyperechoic bands extending to the dermis of the skin with an unclearly appearing deep fascia (DF). Post-physiotherapy the hypodermis showed a more homogenous but coarse echotexture. The superficial fascia appeared hyperechoic with unclear layering. On the transverse scan after physiotherapy there was an arch-like structure causing a shadow which was closely related to the SF and could have been the remnant of the cord.

7.2.4.2. Dynamic

On the left, post-physiotherapy, clear muscle gliding appeared on Video 2.1 between the deep fascia and the muscle and more independent of the more superficial structures. More independent movement was seen after physiotherapy on the right between the fascial layers and the muscle (Video 2.3). The continued adherence of the different layers was, however, visualised in Video 2.4 with a fibrotic structure pulling on the various tissues when moving the arm.

7.2.4.3. Links between outcome measures

Although no clear improvement was visualised post-physiotherapy on the ultrasound scans, possibly due to the radiotherapy, there was a difference in the connection of the superficial fascia to the skin with fewer clear connections and a coarser appearance on the longitudinal scans after the treatment. The findings could be related to the part-resolution of the cord, the slightly reduced tightening and adherence of the skin and improved range of motion and pain scores. Also, a clear difference was noted between affected and unaffected sides with the left, more able side, appearing more continuous and the tissue layers moving independently from another. The finding correlated with the better range of movement of the left side before and after physiotherapy compared to the affected side.

7.3. Patient FS/2013/03

***Table 7.5.** Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	48 years	
Side affected	Left	
Handedness	Right	
Treatments	**Surgery**	Left mastectomy + left ANC
	Chemotherapy	CAF (x6) + Paclitaxel (x6)
	Radiotherapy	42.7 Gy (2.67 Gy/frac) chest wall, medial + superior half axilla of axilla, supraclavicular area
	Hormonal therapy	-
No. of days surgery until presentation	132	
Self-reported symptoms	Pain, cording and reduced range of movement	
Drop-out	Unable to commence with physio due to socioeconomic and personal factors	

***Figure 7.7.** With the arm in the ABER position, showing the cord (arrow) for patient FS/2013/03 after physiotherapy. L=left, R=right.*

7.3.1. Patient description

A 48-year-old woman presented with left cording, tightness and pulling in the axilla and onto the chest wall, pain and limited shoulder movement (Table 7.5, Figure 7.7).

The patient was treated with a left mastectomy and left axillary node clearance for breast carcinoma. Her treatment included neoadjuvant 42.7 Gy radiotherapy to her chest wall, medial + superior half axilla of axilla, supraclavicular area (2.67 Gy/frac) and six courses of CAF and an adjuvant six courses of Paclitaxel which finished on the day of the first measurement cycle.

Due to personal issues she had to drop out of the study subsequent to the first measurement cycle.

7.3.2. Surface anatomy

An obvious finger-thick cord extended over the whole medial axilla from the chest wall into the lateral aspect of the left upper arm when having the arm in the ABER position (Figure 7.7L). It was located over the coracobrachialis muscle. No axillary irregularities were found on the right side.

7.3.3 Measurements

At the first measurement cycle the cord length spanned 100.18 mm in the axilla (Table 7.6). The patient reported high levels of pain (42/50) and moderate disability (65/80) for the SPADI scores which were connected to the cording and tightness of axilla and the inability of the patient to move her arm, scoring 9/10 for most items except for 'washing hair' and 'taking something from back pocket'. Although her functional Fact-B score was higher (20/28), her physical score was very low with 8/28 where she indicated she was out of energy, nauseous and had pain (4/4), corresponding to the SPADI findings.

Table 7.6. *The different scores for the outcome measures of cord length, SPADI and FACT-B.*

Values at first measurement cycle	
Outcome measure	**Before**
Cord length (mm)	100.18
SPADI (pain)	42
SPADI (disability)	65
SPADI (total)	107
FACT-B (physical)	8
FACT-B (social)	28
FACT-B (emotional)	22
FACT-B (functional)	20
FACT-B (additional concerns)	17
FACT-B (total)	95

The patient's range of movement measurements (Figure 4.38) showed limited differences between extension, external and internal rotation but very high differences of 89% for abduction and 157% for forward flexion between affected and unaffected sides. Abduction and forward flexion were therefore the most affected movements, with the unaffected side's ROM falling in the normal range. It correlated with the symptoms of cording, pain and disability in the left arm.

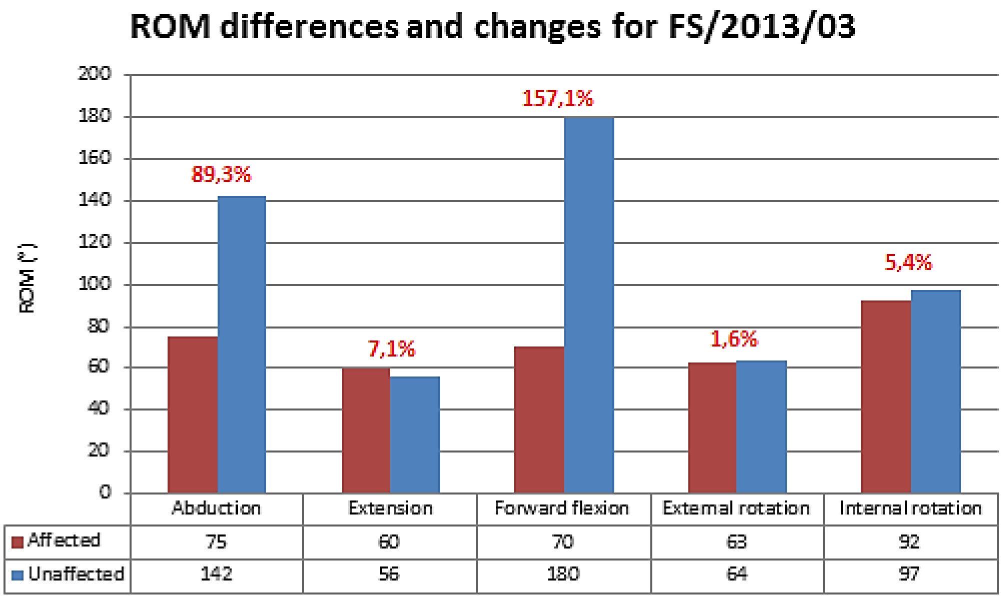

Figure 7.8. *The difference between left and right arms on range of movements for patient FS/2013/03. The left side is highlighted in blue and the right side in red. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference.*

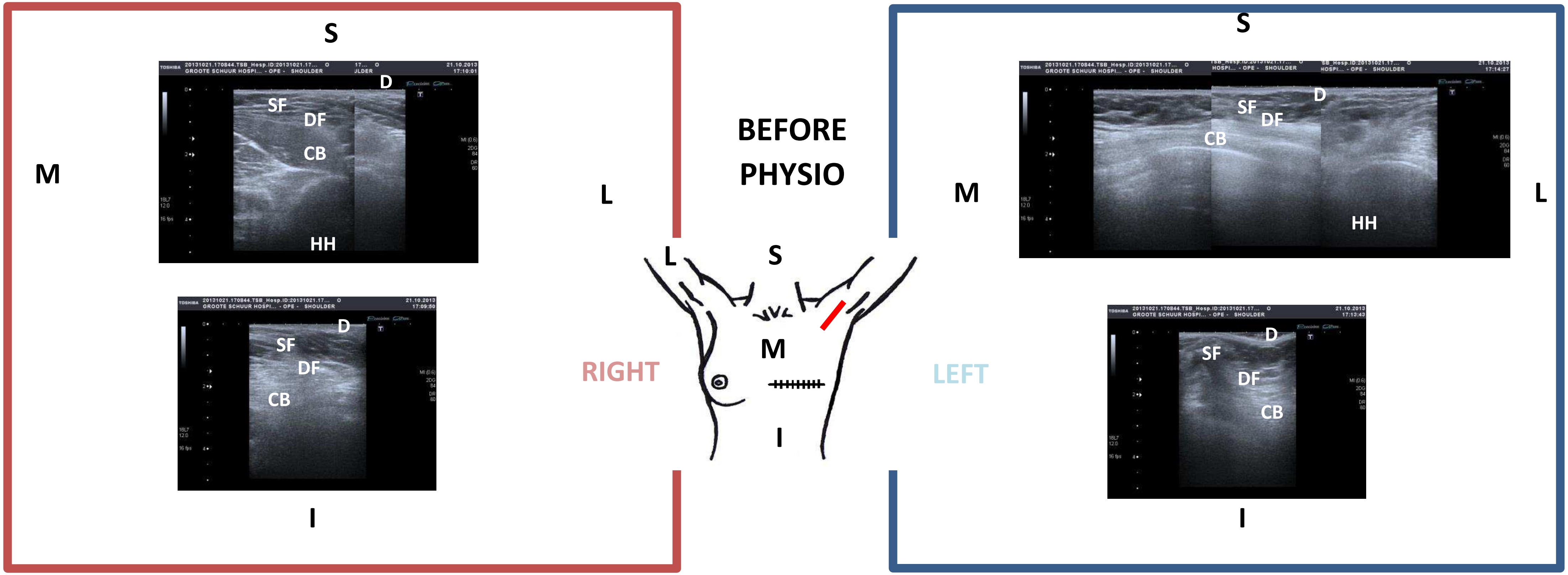

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Plate 7.3.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/03 before physiotherapy as indicated by the torso pictogram. The torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.3.4. Ultrasonography Plate 3

7.3.4.1. Static

7.3.4.1.1. Left

On the left longitudinal scans it was noted that an adipose layer of approximately 1 cm with disrupted and unclearly defined fibres in it that extended towards the skin (D). Herein, the superficial fascia (SF) was showing coarse homogeneity, hyperechogenicity and thickening, relating closely to an even hyperechoic deep fascia (DF) of the coracobrachialis (CB) muscle. The heterogeneous echogenicity of the muscle showed coarse. On the transverse scan there was a shadow of a structure seen below the superficial fascia that extended between 1-2 cm, connected to SF and DF and appeared to arch the skin at the level of the D-marker.

7.3.4.1.2. Right

On the right side with 0.5 cm hypodermis, there was more clearly defined fibre continuity within the adipose tissue layers visible on both the longitudinal as well as the transverse scans. The homogenous echogenicity appeared more diffuse of the muscle. The SF and DF were also more hypoechoic than on the left side.

7.3.4.2. Dynamic

The left (Video 3.1) shows clear hyperechoic strands and increased traction on the skin when moving the arm in the ABER position. There was more independent gliding superficially on the right side (Video 3.2).

7.3.4.3. Links between outcome measures

The disrupted adipose mesh and hyperechoic appearance that was visible on the affected left side seemed related to the surgical disruption which occurred there. The thickened and hyperechoic SF could be indicative of the cord presence as well as the shadowing artefact. The increased traction on the SF and the adherence of the tissue layers when moving were linked to reduced range of shoulder movement and pain.

7.4. Patient FS/2013/04

Table 7.7. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	69 years	
Side affected	Right	
Handedness	Right	
Treatments	**Surgery**	Right mastectomy + right ANC
	Chemotherapy	CEF (x6)
	Radiotherapy	42.7 (2.67 Gy/frac) chest wall, medial and superior half axilla of axilla, supraclavicular area
	Hormonal therapy	Tamoxifen + Arimidex
No. of days surgery until presentation	368	
Self-reported symptoms before	Pain, cording and reduced range of movement	
Self-reported symptoms after	-	
No. of physiotherapy treatments	6	
Physiotherapy focus	Scar massage; scapular mobilisations; myofascial release into the axilla, chest wall and upper arm; cord release; homework stretches	
Confounding factor	Thoracic kyphosis affecting shoulder movement	

Figure 7.9. *With the arm in the ABER position, showing the cord area for patient FS/2013/04 before physiotherapy. L=left, R=right.*

7.4.1. Patient description

A 69-year-old woman presented 368 days post-surgery with axillary cording, pain and limited range of movement (Table 7.7, Figure 7.9).

The patient was treated with a right breast mastectomy and right axillary node clearance for breast carcinoma. The patient received an adjuvant six course CEF regimen of chemotherapy, adjuvant Tamoxifen after which she switched to Arimidex due to the side-effects of Tamoxifen, and 42.7 Gy adjuvant radiotherapy to the chest wall, medial and superior half axilla of axilla, supraclavicular area (2.67 Gy/frac).

The physiotherapist reported a very tight scar on the right chest wall with puckering and increased adherence to the chest wall. She focused on the scar initially to remove the dead skin that was left after radiotherapy and after that she focused on the very rigid scapular movements and myofascial releasing of the chest wall, axilla and upper arm to pectoralis major and minor, coracobrachialis, serratus anterior, upper trapezius and infraspinatus. The patient also presented with a thoracic kyphosis which affected her shoulder movements adversely.

7.4.2. Surface anatomy

Figure 7.9 showed the right tightened axillary fossa with a slight indenting cord more medially (poorly visible on the photographs). It was overlying the coracobrachialis muscle.

After physiotherapy, the cord was resolved at the time of the second measurement cycle, visible in Figure 7.10, where the right arm was less restricted and the axilla less tightened. The physiotherapist mentioned, however, that she still observed a cord remnant at full elevation a few days before the second measurement cycle.

Figure 7.10. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/04 after physiotherapy. L=left, R=right.*

7.4.3. Measurements

At the first measurement cycle, the axillary cord measured a length of 92.64 mm on the right side, which had (according to our measurements) fully resolved after physiotherapy (Table 7.8).

The patient reported much less pain (-67.7%) at the second measurement cycle with the biggest improvement on the item 'reaching high' (8 to 1). Her SPADI disability score, however, remained the same with no improvement on items "putting an object on a high shelf" and slightly more difficulty with 'carrying heavy objects' (2 to 3) or 'washing her back' (2 to 4). The disability score findings could perhaps be explained by the physical sub-domain Fact-B score where she indicated that she had less energy and was more bedridden at the time of the second measurement cycle. Her overall FACT-B score was also only slightly improved even though she had much less pain with her movements.

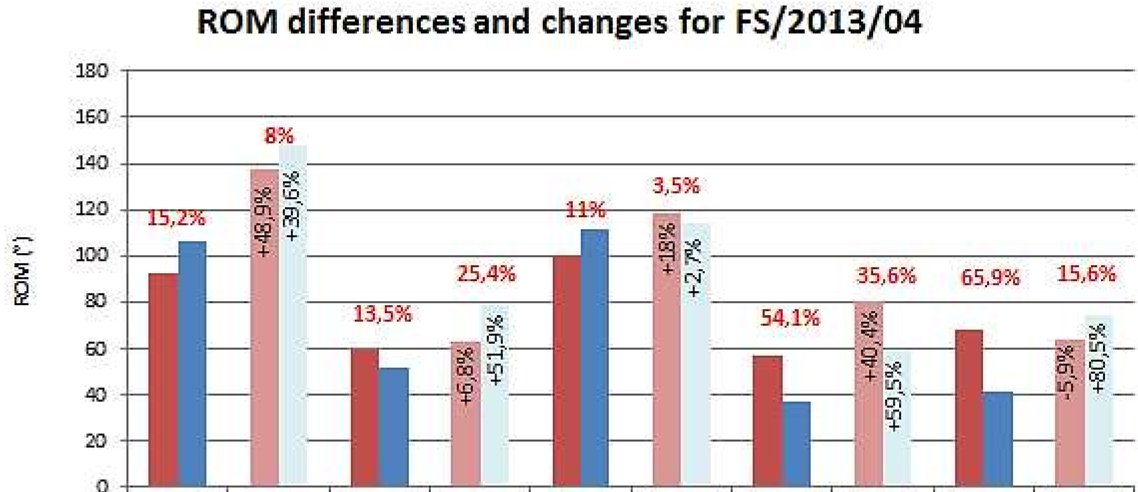
Table 7.8. *Percentage change of cord length, SPADI and FACT-B scores after physiotherapy.*

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	92.64	0	**-100**
SPADI (pain)	21	7	**-66.7**
SPADI (disability)	17	17	**0**
SPADI (total)	38	24	**-36.8**
FACT-B (physical)	20	17	**-15**
FACT-B (social)	28	25	**-10,7**
FACT-B (emotional)	14	15	**+7.1**
FACT-B (functional)	22	25	**+13.6**
FACT-B (additional concerns)	23	29	**+26.1**
FACT-B (total)	107	110.5	**+3.3**

The patient's range of movement (Figure 7.11), like her pain score, also showed improvements after physiotherapy for all movements except internal rotation on the affected arm, with only a couple degrees difference. Her biggest improvement was in abduction on the affected arm with a 48.9% increase, although her unaffected arm also increased by almost 40%.

Interestingly, her extension and internal rotation measurements on the affected side were higher than on the unaffected arm. The ROM measures changed around after physiotherapy for extension, but for external rotation there was still a 35.6% difference between affected and unaffected with a higher range of movement for the affected arm.

Apart from extension, the differences between each movement was reduced, indicating both arms were more similar. The differences still presented and her disability could be due to some residual tightness and her thoracic kyphosis which could have reduced some of her shoulder movements.



	Abduction	Abduction after	Extension	Extension after	Forward flexion	Forward flexion after	External rotation	External rotation after	Internal rotation	Internal rotation after
Affected	92	137	59	63	100	118	57	80	68	64
Unaffected	106	148	52	79	111	114	37	59	41	74

Figure 7.11. *The difference between left and right arms and improvement on range of movements for patient FS/2013/04 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*

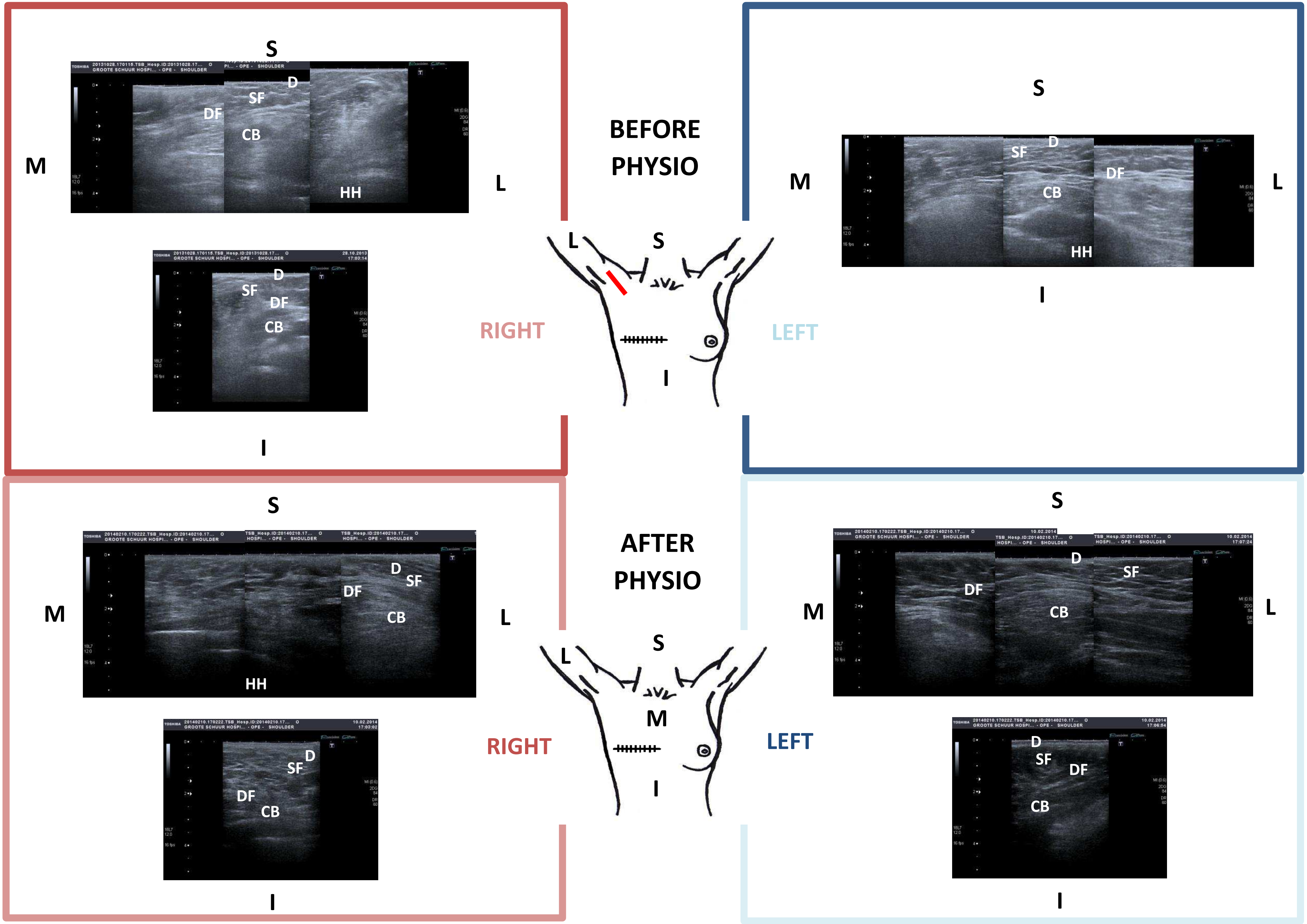


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Plate 7.4.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/04 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.4.4. Ultrasonography Plate 4

7.4.4.1. Static

7.4.4.1.1. Left

On the left longitudinal ultrasonograph there was an adipose tissue layer of approximately 2 cm present. The superficial fascia (SF) was clearly defined and multi-layered, continuing throughout the scans. It was connected to the deep fascia (DF) and to the dermis (D). The strands were clearly visible although there was some coarse heterogeneous echotexture visible. Post-physiotherapy there was little difference, portraying similar organisation as before on both longitudinal as well as the transverse scan, although more defined.

7.4.4.1.2. Right

On the right longitudinal scans there was a lot more disruption visible in the fascial layers of the hypodermis (± 2 cm) and the SF was scarce. A couple of thickened SF fibres floated in between a dotted coarse homogenous echotexture. There appeared to be very close association with the dermis on the transverse scan with the superficial fascia extending around a shadowy artefact. The DF also seemed increased in thickness on both scans. After physiotherapy there appeared some more regularity and organisation in fascial layering on especially the transverse scan, but there still seemed to be increased coarse homogenous echotexture on the affected side compared to the unaffected side.

7.4.4.2. Dynamic

On the left side there was linearity within the hypodermal fascial layers and independent movement of the coracobrachialis muscle before and after physiotherapy but more clearly seen after physiotherapy (Video 4.1 before, Video 4.2 after). On the right, however, before physiotherapy there appeared to be much more connectivity between the different tissue layers which moved as one when the arm was in motion (Video 4.1). After physiotherapy there was more independent muscle gliding although the hypodermis still appeared disrupted (Video 4.2).

4.11.4.4.3. Links between outcome measures

The affected side showed no cord structure on the ultrasound scans but disrupted fascial layering within the hypodermis, thickening of the SF and DF and increased connections between the layers that were possibly associated with restricted movement or pain, as experienced by the patient. After physiotherapy movement improved with increased muscle gliding correlating to the improvements in the shoulder range of movement.

7.5. Patient FS/2013/05

Table 7.9. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	35 years	
Side affected	Left and right	
Handedness	Right	
Treatments	**Surgery**	Bilateral mastectomy + bilateral ANC
	Chemotherapy	CAF (x6) + CMF (x6)
	Radiotherapy	-
	Hormonal therapy	Tamoxifen + Arimidex
No. of days surgery until presentation	201	
Self-reported symptoms before	Cording and pain	
Drop-out	Possible cord resolution but socioeconomic and personal factors prevented the patient from participating in the present study	
Challenges	Language barrier	

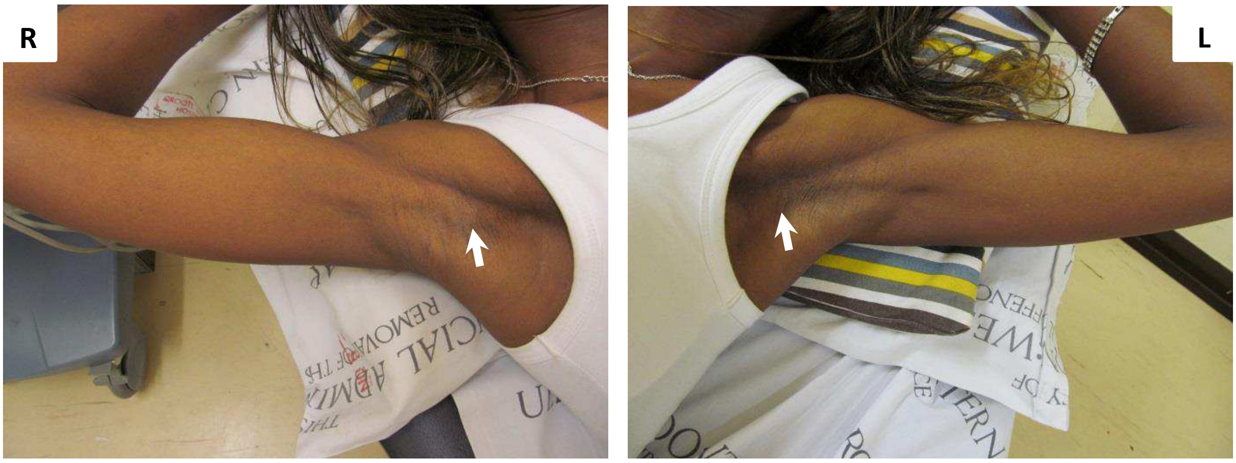

Figure 7.12. *With the arm in the ABER position, showing the indistinct cords (arrow) for patient FS/2013/05. L=left, R=right.*

7.5.1. Patient description

A 35-year-old patient presented 201 days post-surgery with tightness in the axilla and taut bands of tissue that caused pain upon movement of the arm. The patient did not complain about limited range of movement (Table 7.9, Figure 7.12).

The patient was treated with a bilateral mastectomy and bilateral axillary node clearance for breast carcinoma. She received neoadjuvant chemotherapy of six CAF and six CMF regimens and after that neoadjuvant Tamoxifen. Post-surgery she started with Arimidex.

When seen by the physiotherapist a few days later, no clear cording was identified on either arm, although tightness and pulling were observed more on the left than on the right side. Also, there were some problems filling in the questionnaires due to a language barrier even though she spoke English and her questionnaire was translated into isiXhosa.

7.5.2. Surface anatomy

Figure 7.12 showed a taut band or cord extending on the left (L) from the axillary fossa retracting the skin inwards through the vascular groove and fanning out towards the biceps brachii and medial side of the arm. On the right (R) it was more indistinct and thinner, causing not as much traction on the skin in the ABER position, but lying in the same area of the axilla.

7.5.3 Measurements

At the first measurement cycle, the patient's cord/taut band measured 133.23 mm on the left and 72.51 mm on the right arm. Although the patient's cord length was longer and tightness seemed to be located more on the left than the right, she reported the same amount of pain on the right as on the left arm and limited disability on both sides (Table 7.10). She seemed to have more problems with 'reaching high' in terms of pain on the left (10/10) compared to the right (0/10), but had trouble for both arms when asked to 'put an object on a high shelf' (10/10).

The patient's FACT-B score showed a reduced physical domain with high scores for lack of energy and having pain (4/4), but higher functional domain score which mirrored her own functional ability.

Table 7.10. *The different scores for the outcome measures of cord length, SPADI and FACT-B.*

Values at first measurement cycle	
Outcome measure	**Before**
Cord length (mm)	L: 133.23/ R: 72.51
SPADI (pain)	L: 30 / R: 30
SPADI (disability)	L: 20 / R: 20
SPADI (total)	L: 40 / R: 50
FACT-B (physical)	16
FACT-B (social)	20
FACT-B (emotional)	16
FACT-B (functional)	21
FACT-B (additional concerns)	18
FACT-B (total)	90.8

There was little difference in abduction, forward flexion and internal rotation, although the forward flexion was more limited compared to normal ranges (120 versus 180) (Figure 7.13). Although there was a 10% difference in extension, the actual degree difference was only 5% and thus very small. External rotation, however, showed a more substantial difference with a 23% higher score on the right compared to the left. The ROM difference between arms was in agreement with the longer cord and increased tightness observations for the left side.

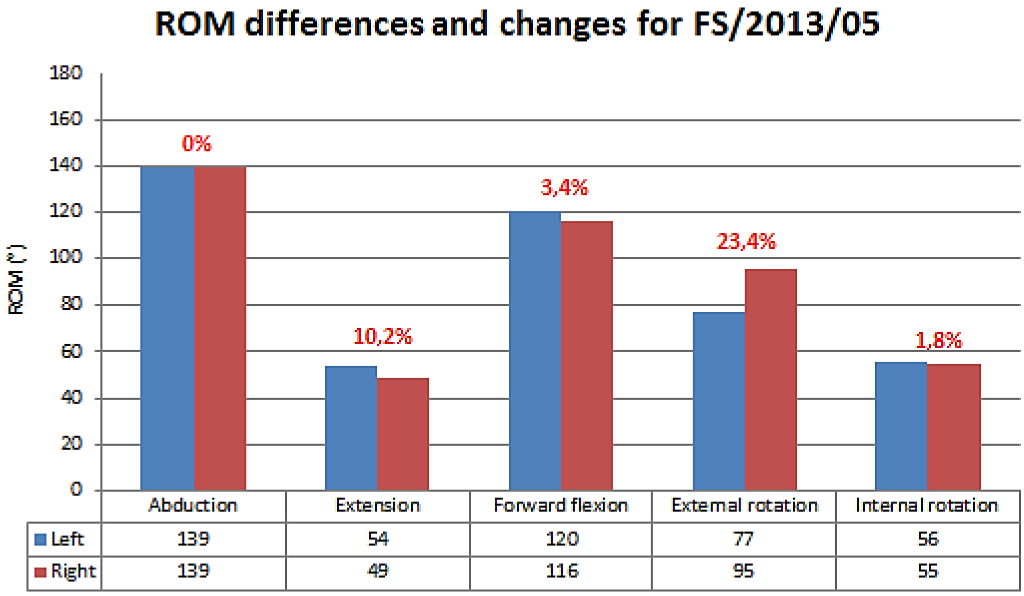

Figure 7.13. *The difference between left and right arms of movements for patient FS/2013/05. The left side is highlighted in blue and the right side in red. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference.*

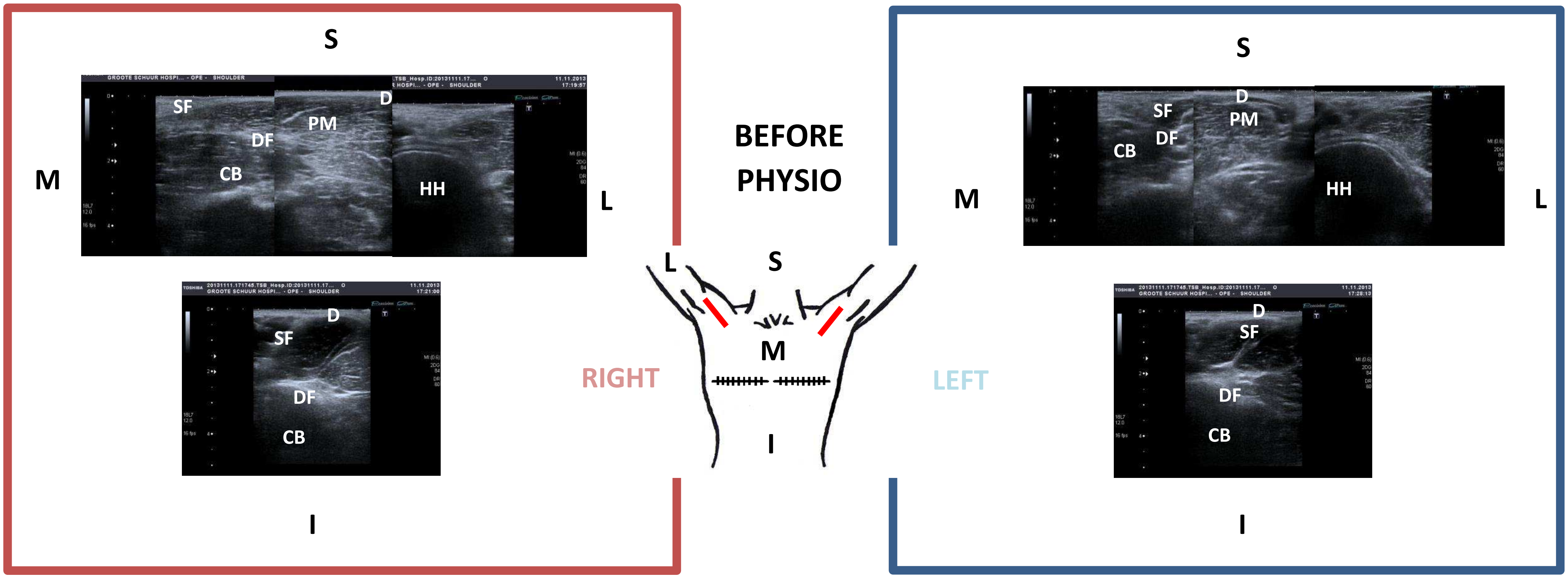
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Plate 7.5.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/05 before physiotherapy as indicated by the torso pictogram. The torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, PM=pectoralis major muscle, HH=humeral head.

7.5.4. Ultrasonography Plate 5

7.5.4.1. Static

7.5.4.1.1.Left

The left adipose layer was very limited to 0.1-0.5 cm on the selected scans and showed as patches of tightly packed coarse hyperechoic, homogenous echotexture near the dermis. Within the superficial adipose tissue there was no completely clearly defined superficial fascia (SF) layering present. There was a haphazard meshwork of hyperechoic connective tissue strands between the muscles (coracobrachialis=CB, pectoralis major=PM) and lining them (deep fascia=DF). The PM showed increased connectivity and connective tissue. On the transverse scan there was a stellate-shaped conglomeration of hyperechoic connective tissue found at the meeting point of the SF and DF which connected strongly to the skin and muscular fascia.

7.5.4.1.2. Right

On the right there was greater definition of the coracobrachialis muscle. The adipose tissue of similar thickness as the left, also showed patches of coarse hyperechoic, homogenous echotexture as seen on the left but there seemed to be more definition of layering in the SF. There was similar disruption of the tissue layering as on the left but there seemed to be greater organisation in the central image with multiple hyperechoic strands deriving from the DF into the PM. On the transverse scans there was once again a thickened fibrotic scar seen as continuation of the deep DF but with less connection to the SF.

7.5.4.2. Dynamic

On Video 4.5.1 showing the movement into the ABER position on the left, there was not very much gliding potential between the different tissue layers, although difficult to observe from the video. A hyperechoic strand deriving from a thickening near the humeral head was exerting traction on the dermis with the action of moving the arm in the ABER position.

On the right (Video 5.2) there was more gliding between the pectoralis major muscle, the skin and underlying tissue layers.

7.5.4.3. Links between outcome measures

Although it was unclear whether there was clear cording present in the patient, there were differences found between the left and right. As shown in Figure 7.12, there was increased tightness and a band of tissue which was measured to be longer than a similar, although less distinct one, on the right. The patient reported, for both left and right side, more pain than disability, showing as very little differences on the ROM measures, but relating to the tightness in the axillae.

On the US scans it was noted that there was a strong hyperechoic connection from the DF to the skin on the left and more disrupted SF on the left with limited gliding potential compared to the right. The restricted gliding correlated to the tightness, skin adherence and limited external rotation movement as part of the ABER position, although no cord was visible on the scans.

7.6. Patient FS/2013/06

Table 7.11. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	55 years	
Side affected	Right	
Handedness	Right	
Treatments	**Surgery**	Right mastectomy + right ANC
	Chemotherapy	CAF (x6) + Vinorelbine (x6)
	Radiotherapy	47 Gy (2.35 Gy/frac) chest wall, medial and superior half axilla of axilla, supraclavicular area; 20 Gy (4 Gy/Frac) superior half axilla of axilla, supraclavicular area
	Hormonal therapy	Tamoxifen + Exemestane + Arimidex + Provera
No. of days surgery until presentation	57 days	
Self-reported symptoms before	Cording, pain and limited range of movement	
Drop-out	Commenced physiotherapy but was too ill to continue due to progressive disease	
Challenges	Increased BMI	

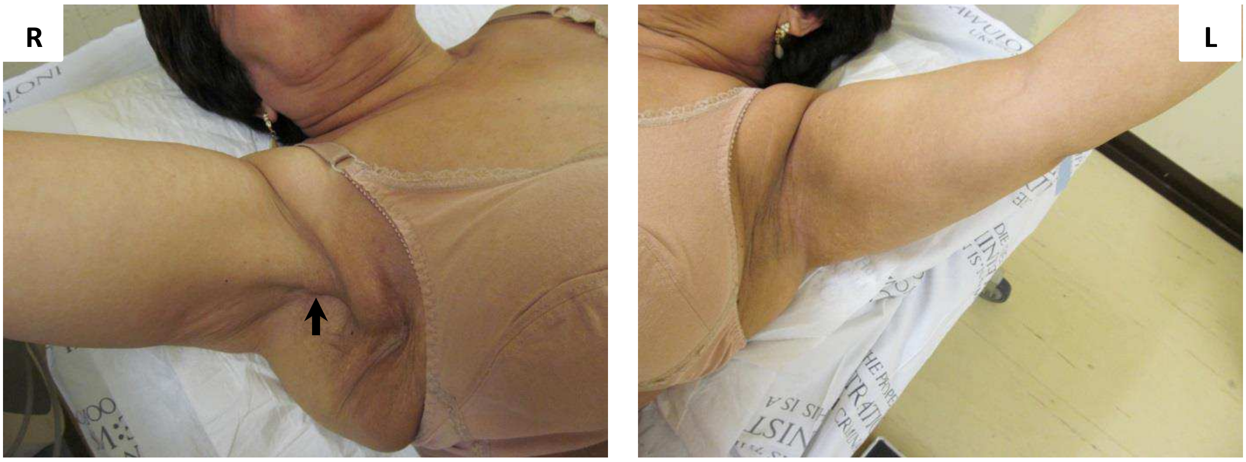


Figure 7.14. *With the arm in the ABER position, showing the cord (arrow) for patient FS/2013/06. L=left, R=right.*

7.6.1 Patient description

A 55-year-old woman presented 57 days after surgery with reduced range of movement, axillary webbing and pain when moving the right arm (Table 7.11, Figure 7.14).

The patient was treated with a right mastectomy and right axillary node clearance for breast carcinoma. The patient also received neoadjuvant six courses of CAF and changed from Tamoxifen to Exemestane. She received 47 Gy radiotherapy to the chest wall, medial and superior half axilla of axilla (2.35 Gy/frac). She then started on Arimidex, had 20 Gy radiotherapy to the supraclavicular area and superior half axilla of axilla (4 Gy/Frac). Subsequently, she had six courses of Vinorelbine (which she continued during the physiotherapy treatment) and had adjuvant Provera for hormonal treatment.

Even though she had started receiving physiotherapy treatment under the auspices of the study, she could not continue due to progressing cancer.

7.6.2. Surface anatomy

A web of skin folds was observed on the right arm with one finger-thick taut cord bulging out at the level of the axillary vascular groove (Figure 7.14). The thickness of the cord was exaggerated due to the higher amount of adipose tissue in the hypodermis. The indenting skin forming the separate skin folds was adherent to the underlying tissue.

7.6.3 Measurements

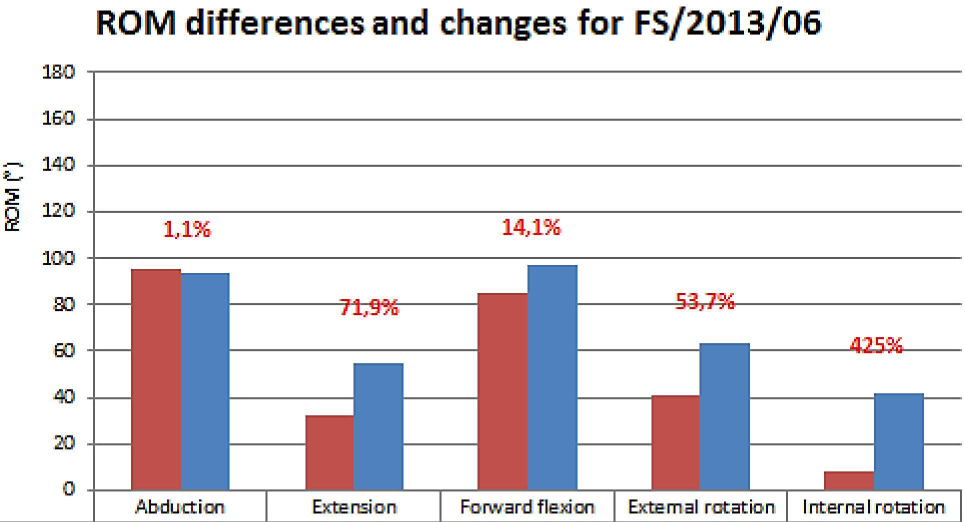
At the first measurement cycle the cord measured 71.19 mm and the patient experienced moderate amounts of pain and high levels of disability according to her SPADI answers (Table 7.12), reporting the highest amount of pain when reaching for something high (8/10). Her disability was exemplified by the high difficulty experienced when 'washing her back', 'reaching for an object on a high shelf' and 'carrying heavy objects' (10/10).

The patient had a very low FACT-B physical score of 8/24 indicating low energy levels (3/4) and feeling ill (4/4).

Table 7.12. *Percentage change of cord length, SPADI and Fact-B scores after physiotherapy*.

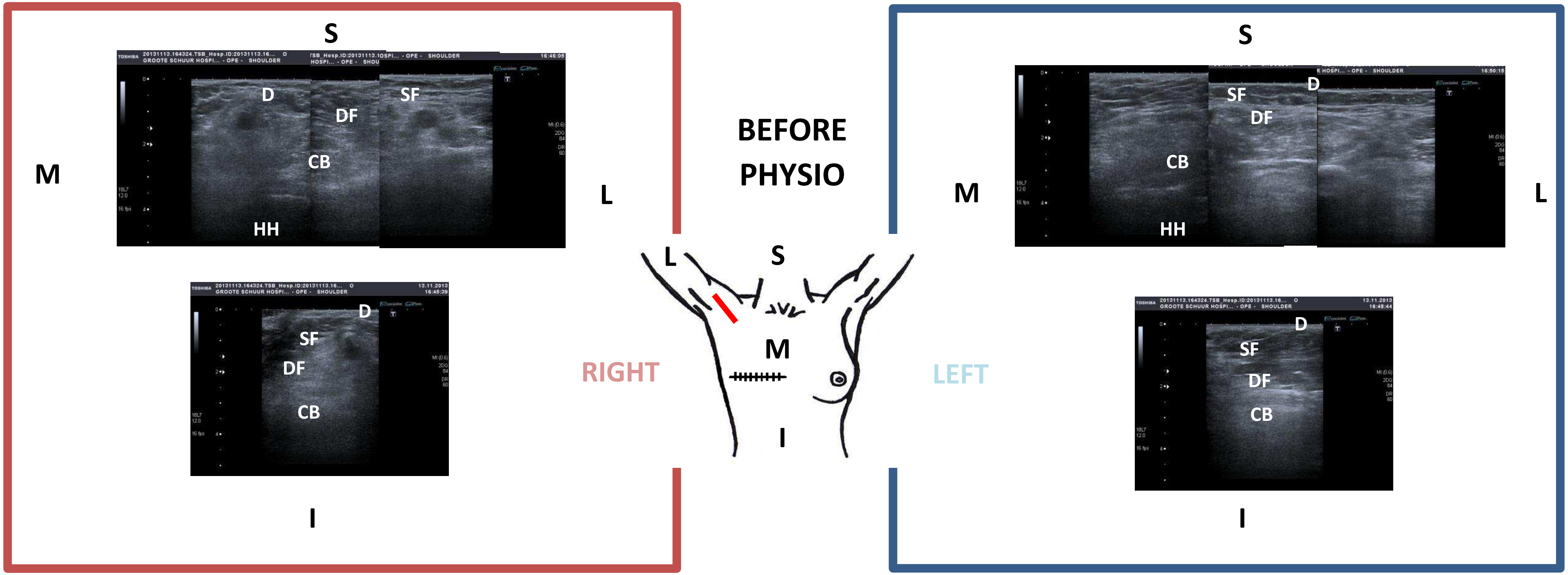
Changes after physiotherapy	
Outcome measure	**Before**
Cord length (mm)	71.19
SPADI (pain)	33
SPADI (disability)	61
SPADI (total)	94
FACT-B (physical)	8
FACT-B (social)	28
FACT-B (emotional)	20
FACT-B (functional)	18
FACT-B (additional concerns)	19
FACT-B (total)	93

Figure 7.15 showed that all movements on the affected side were lower than on the unaffected side except for a minor difference in abduction. Apart from extension, all unaffected movements were also lower than the expected normal range. The most affected action seemed to be internal rotation where the unaffected side was 425% higher than the affected side. The reduction related to the presence of the web of tight tissue and cord in her axilla, preventing her from normal arm functioning and was linked to the pain and disability as identified by SPADI.



	Abduction	Extension	Forward flexion	External rotation	Internal rotation
Affected	95	32	85	41	8
Unaffected	94	55	97	63	42

Figure 7.15. *The difference between left and right arms and improvement on range of movements for patient FS/2013/06 after physiotherapy. The left side is highlighted in blue and the right side in red. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference.*



BEFORE
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D
SF
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Plate 7.6.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/06 before physiotherapy as indicated by the torso pictogram. The torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.6.4. Ultrasonography Plate 6

7.6.4.1. Static

7.6.4.1.1. Left

On the left longitudinal ultrasound scans an adipose tissue layer of approximately 1.5-2 cm was noted. The superficial fascia (SF) planes were more defined and continuous, extending superficially and to the deep fascia (DF). There was no complete homogenous echogenicity within the muscle (CB) and no linearity of the endomysial fascia surrounding the fascicles either. The transverse scan showed an unbroken SF and a slightly unclear DF overlying the CB.

7.6.4.1.2. Right

On the right, a more disrupted but similar thickness hypodermis with a meshwork of thickened fibres and unclear SF, that was in many places connected to the dermis and DF, was observed. The muscle fascicles within the muscles were also not arranged perpendicularly. On the transverse scan less organisation was observed compared to the left, where there was no distinctive DF and the SF was surrounding another such lesion and connecting to the dermis.

7.6.4.2. Dynamic

On Video 6.1 the left side showed regularity and continuity of the fascial layers that was clearer than the static scans. During movement there also appeared to be more independence with muscle gliding although it was not very clear on the video. Video 6.2, on the contrary, showed more adherence of all layers to one another and the dermis when the arm was moved. There were also disrupted fibrotic strands within the SF which seemed to extend through to the DF.

7.6.4.3. Links between outcome measures

The disarrangement as seen on the surface of the right axilla with the skin folds continued into the hypodermis on the ultrasonographs where the superficial fascial layers were discontinuous and showed adherence of the deeper fascia and muscle to the skin. Potential muscle and other tissue gliding loss as seen on the Video was furthermore associated with the limited movement, especially of the affected arm, ~~and~~ as well as disability and pain measures.

7.7. Patient FS/2013/07

Table 7.13. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	63 years	
Side affected	Right	
Handedness	Right	
Treatments	**Surgery**	Right mastectomy + right ANC
	Chemotherapy	CAF (x6)
	Radiotherapy	47 Gy (2.35 Gy/frac) chest wall, medial and superior half axilla of axilla, supraclavicular area
	Hormonal therapy	Tamoxifen
No. of days surgery until presentation	798 days	
Self-reported symptoms before	Pain, cording, reduced range of movement	
Self-reported symptoms after	-	
No. of physiotherapy treatments	5	
Physiotherapy focus	Tightness in axilla; myofascial release of chest wall, scar, axilla and upper arm; scapula mobilisation	
Confounding factor	Thoracic kyphosis affecting shoulder movement	

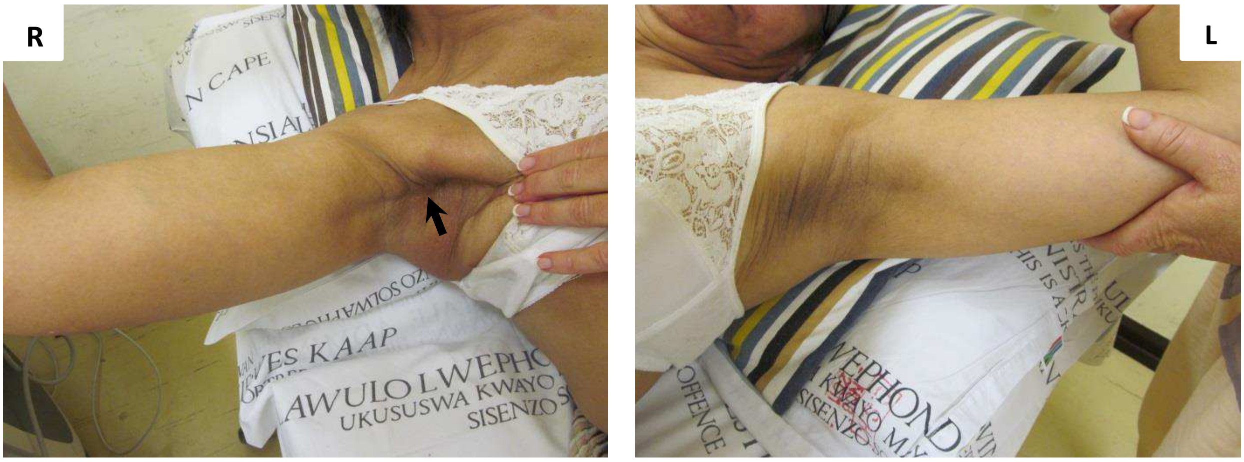

Figure 7.16. *With the arm in the ABER position, showing the cord area (arrow) for patient FS/2013/07 before physiotherapy. L=left, R=right.*

7.7.1 Patient description

A 63-year-old patient presented 798 days post-surgery with a cord on the right side, pain upon movement and limited shoulder range of movement (Table 7.13, Figure 7.16).

The patient was treated with a right breast mastectomy and right axillary node clearance for breast carcinoma. Adjuvant treatment included six courses of the CAF regimen, tamoxifen and 47 Gy radiotherapy to the chest wall, medial and superior half axilla of axilla, supraclavicular area (2.35 Gy/frac).

The physiotherapist reported an increased tightness in the axilla and a taut band of tissue in the affected axilla. The patient also felt a pull further down the upper arm across the cubital fossa although no superficial sign was observed, and a pain inside the arm towards the thumb. The patient was very anxious not to use the affected arm and guarded it beyond 90° elevation. Furthermore, the patient had a 'hunchback', thoracic kyphosis, which limited her shoulder movement.

The focus of the physiotherapy treatment was to release the tightness in the axilla, in the upper arm and on the chest wall via myofascial release of pectoralis major and minor, serratus anterior and extended down the forearm to the flexor retinaculum, and improved scapula mobilisation.

7.7.2. Surface anatomy

Figure 7.16 showed a very tight axilla with a taut band retracting the skin inwards extending from the medial axilla inferiorly into the medial aspect of the upper arm superiorly. The band overlaid the coracobrachialis muscle.

After physiotherapy the cord resolved upon measurement, although the physiotherapist reported a small remnant still visible days before (Figure 4.47). Also noticed was the shoulder asymmetry on Figure 7.17c and 7.17d where a clearly hypertrophied trapezius was visible on the left side, and the patient's left range of movement appeared more restricted on the left side compared to the right side.

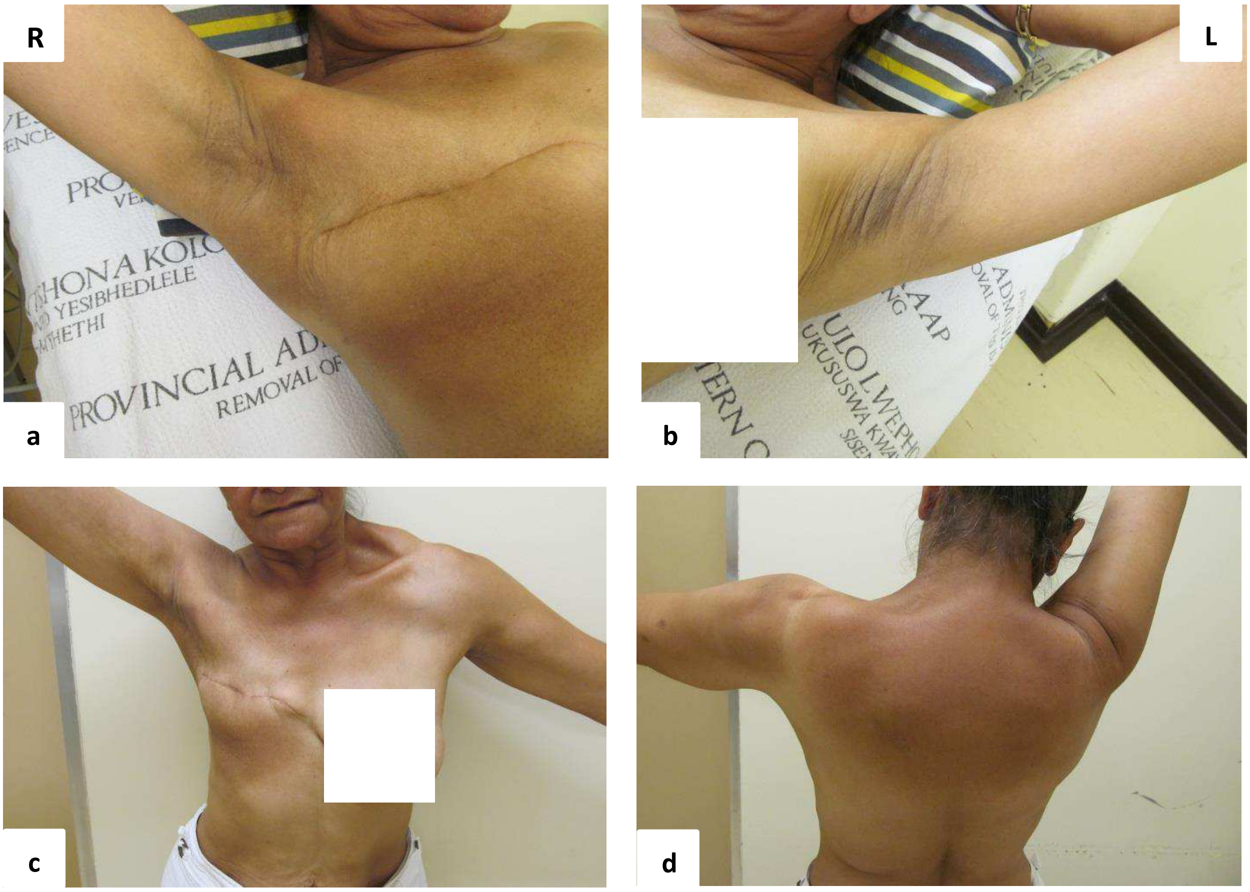

Figure 7.17. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/07 after physiotherapy (a,b) and in abduction her asymmetrical shoulder range of movement, possibly due to the thoracic kyphosis, from the front (c) and the back (d). L=left, R=right.*

At the first measurement cycle her cord measured 70.17 mm in length across the axilla, which completely resolved after physiotherapy treatment (Table 7.14).

An improvement was also noticed in the SPADI pain and disability scores, where, on the affected arm, the patient showed a reduction of approximately 40% in both scores. She still had pain 'when lying on the involved side' and had difficulty 'putting an object on a high shelf' or 'carrying a heavy object', but the item scores reduced to 2 or 3/10, possibly related to some tenderness and tightness still present within the axilla.

The patient's quality of life score also improved with 12.8% as indicated by the total Fact-B score with the improvements in especially the additional concerns section where she indicated less anxiety and less tenderness or swelling in the arm and more energy but still reported having pain in the physical subsection.

Table 7.14. *Percentage change of cord length, SPADI and FACT-B scores after physiotherapy.*

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	70.17	0	**-100**
SPADI (pain)	21	12	**-42.9**
SPADI (disability)	13	8	**-38.5**
SPADI (total)	34	20	**-41.2**
FACT-B (physical)	21	25	**+19**
FACT-B (social)	28	28	**0**
FACT-B (emotional)	22	24	**+9.1**
FACT-B (functional)	27	28	**+3.7**
FACT-B (additional concerns)	19	27	**+42.1**
FACT-B (total)	117	132	**+12.8**

The patient's ROM of both shoulders also improved after physiotherapy, but the affected arm in every action improved more than the unaffected arm and resulted in a higher range of movement (Figure 7.18). The improvement was especially clear in abduction where the affected arm improved with 97% and there was a difference of 67.1% between both arms after physiotherapy. The difference correlated with the reduced pain and disability and the unaffected shoulder being restricted due to the thoracic kyphosis.

After physiotherapy all actions were still below the normal range of movement (Clarkson & Gilewich, 1989).

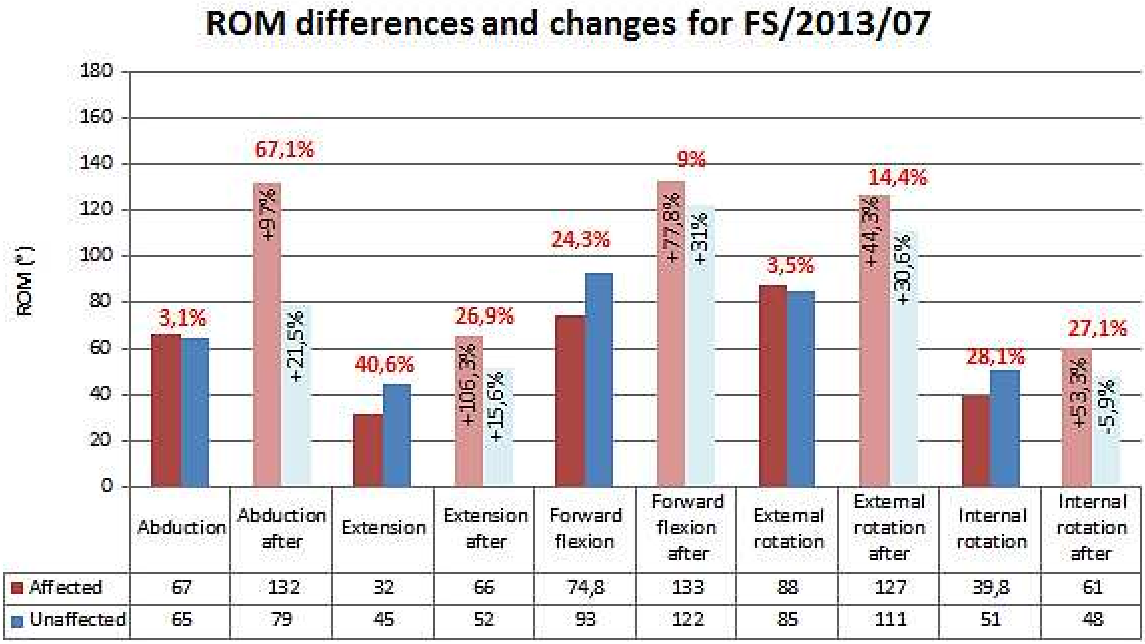

Figure 7.18. *The difference between left and right arms and improvement on range of movements for patient FS/2013/07 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*

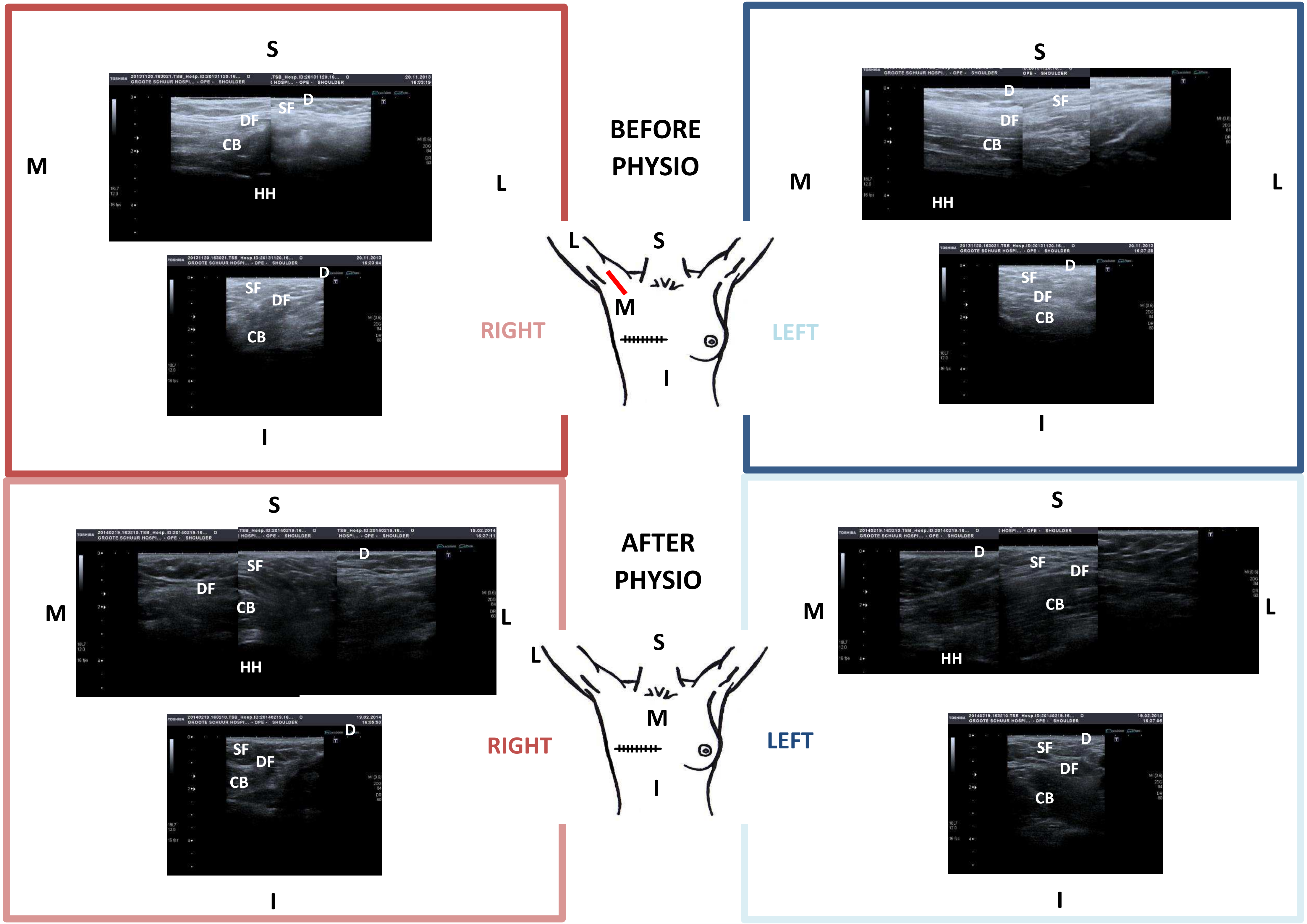

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Plate 7.7.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/07 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.7.4. Ultrasonography Plate 7

7.7.4.1. Static

7.7.4.1.1. Left

On the left longitudinal ultrasound scan there was approximately 0.5-1 cm of adipose tissue present. Within the adipose tissue the superficial fascia (SF) was clearly defined with a multi-layered continuous appearance and had a homogenous echotexture throughout. The deep fascia (DF) was also continuous and closely associated with the SF and the coracobrachialis muscle (CB) showed linearly arranged muscular fibres, although some patches of increased connective tissue were present. On the transverse scan the SF was organised like a honeycomb structure surrounding the vessels with continuity. There was little change post-physiotherapy with reduced echogenicity of the SF and reduced thickness.

7.7.4.1.2 Right

On the right longitudinal scans there was decreased continuity with the SF but it appeared thicker and had increased connectivity with the dermis. The echotexture also appeared homogenous but coarser compared to the left. The muscle fibres were also not as clearly defined with shadowy artefacts, possibly due to scanning error, present. On the transverse scan there was similarly less organisation compared to the left. The organisation appeared to improve post-physiotherapy with more linearity and continuity in the superficial fascia which had a more honeycomb appearance.

7.7.4.2. Dynamic

On the affected arm the videos mirrored the findings above with increased connectivity before the physiotherapy treatment, with thicker superficial fascial strands and reduced gliding of the muscle (Video 7.1) and after physiotherapy, more organisation and layering, less adhesions of the SF and some improved muscle gliding (Video 7.2). On the unaffected arm there was slightly more fluid muscle movement and increased gliding potential but less coarse homogenicity within the CB with more linear epimysial fascia compared to before (Video 7.3 before, Video 7.4 after).

7.7.4.3. Links between outcome measures

As the cord resolved, pain and disability measures as well as the ROM improved on the affected side as well as improved regularity and continuity of the SF, decreased adhesions to the dermis and improved muscle gliding. The unaffected arm also showed some reduced thickening of the fascial fibres and less coarseness correlating with improved functioning but the remaining limitation in ROM on the unaffected side was not visible on the ultrasound scans as it was most likely caused by the thoracic kyphosis and muscular problems around the site of investigation.

7.8. Patient FS/2013/08

Table 7.15. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	68 years	
Side affected	Right	
Handedness	Right	
Treatments	**Surgery**	Right mastectomy + right ANC
	Chemotherapy	CEF (x3) + Taxotere (x3)
	Radiotherapy	NA
	Hormonal therapy	Tamoxifen + Arimidex
No. of days surgery until presentation	1455 days	
Self-reported symptoms before	Cording and pain	
Self-reported symptoms after	Cording and pain	
No. of physiotherapy treatments	6	
Physiotherapy focus	Altered scapulothoracic movement; deep scar massage; myofascial release into axilla, upper arm, scar; homework exercises	
Confounding factors	• Length of time since surgery so tissues not responsive to change • General OA and fibromyalgia • Increased BMI • Lack of motivation home exercises or massage • Lower back pain	

Figure 7.19. *With the arm in the ABER position, showing the cord (arrow) and scar area for patient FS/2013/08 before physiotherapy. L=left, R=right.*

7.8.1. Patient description

A 68-year-old patient presented 1455 days post-surgery with a cording on the right arm and pain upon movement (Table 7.15, Figure 7.19).

The patient was treated with a right mastectomy and right axillary node clearance for breast carcinoma. Her adjuvant treatment included three courses of the CEF regimen and three courses of Taxotere, and hormonal drugs Tamoxifen and Arimidex. According to the physiotherapist the patient mentioned she had also received radiotherapy to the chest wall but which could not be verified from the patient folder.

The physiotherapist worked on the extensively adherent scar incision on the right medial chest wall that extended to the axilla and focused here with myofascial release as well as into the arm and on the cord. Although homework exercises were taught, the patient did not actively do the exercises to maintain the improvements. The physiotherapist mentioned the patient complained of bilateral shoulder pain that was worse on the right, had a slipped disc in her lower back which also caused pain, and suffered from fibromyalgia.

Subtle changes were noticed post-physiotherapy by the physiotherapist across the axilla and marginal reduction of the skin fold thickenings superior to the incision, despite some confounding factors (Table 7.15).

7.8.2 Surface anatomy

In Figure 7.19 a finger-thick cord was visible on the right prominently bulging outwards extending from the scar incision into the medial aspect of the upper arm, lying in the mid-axillary line. The skin folds were the result of the adherent scar lines and the increased BMI. The scar was shown to indent the skin adhering closely to the chest wall.

Post-physiotherapy the arm appeared to be freer in motion, but the cord did not improve and was still very visible and protruding out (Figure 7.20a) as also shown in the first and last physiotherapy comparison photographs (Figure 7.20c-d).

7.8.3 Measurements

At the first measurement cycle the patient's cord measured 68.16 in the axilla which instead of increasing, measured 79.04 mm after physiotherapy (Table 7.16). The increased length may have been due to the cord becoming more exposed upon increased movement.

The patient's shoulder pain and disability scores improved over 70% after physiotherapy, with some residual pain when reaching high and still a lot of difficulty with 'carrying heavy objects' (10/10) with the affected arm. Her FACT-B score on the other hand decreased with 16.8%, which was especially evident in her physical score where she indicated that she had a 'lack of energy', was 'worried about the needs of her family' and she felt 'bedridden', and arguably being related to her other ailments.

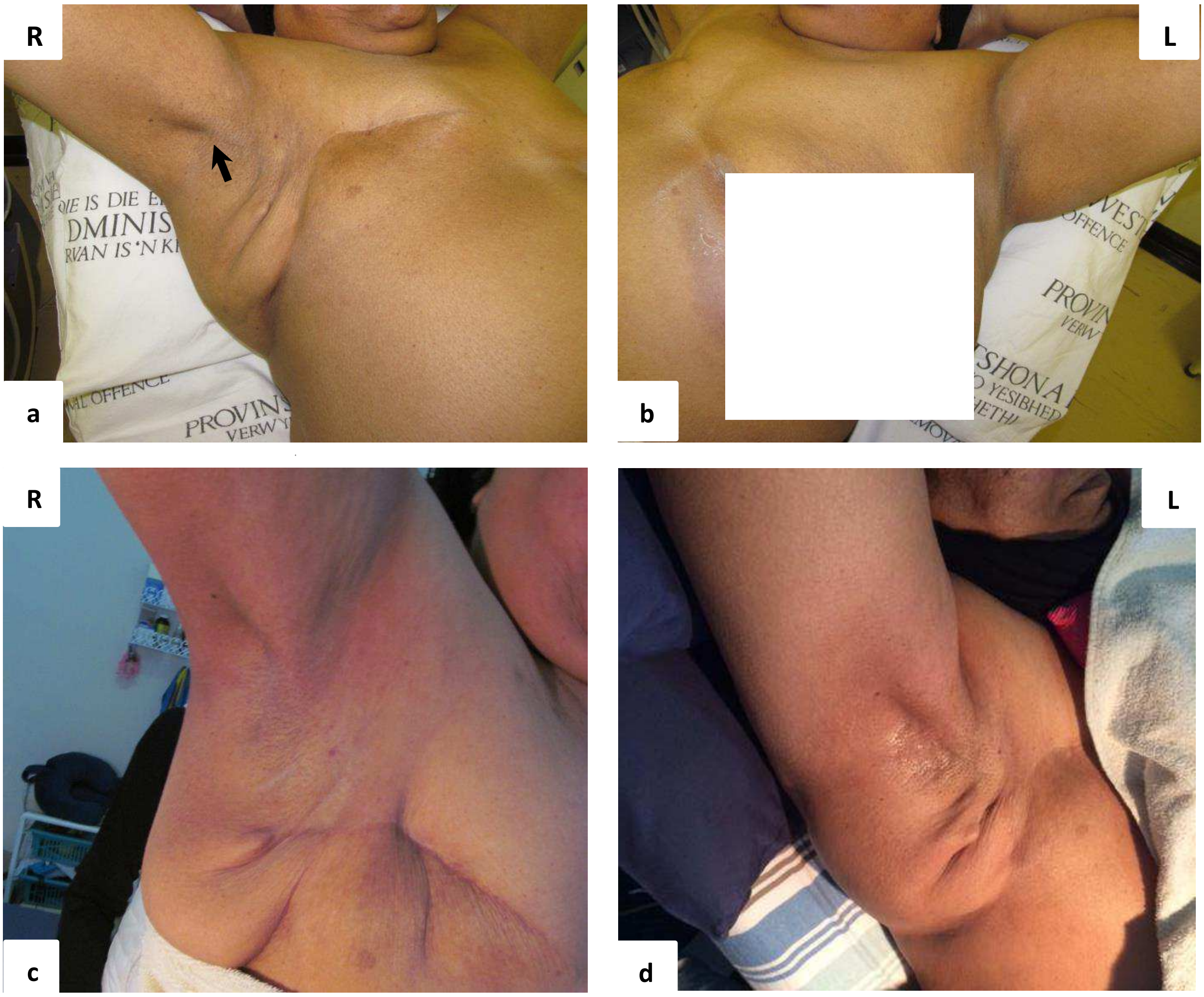

Figure 7.20. *With the arm in the ABER position, showing the cord (arrow) and scar area for patient FS/2013/08 after physiotherapy (a,b) and in abduction of the area at the first (c) and the last physiotherapy treatment (d). L=left, R=right.*

Table 7.16. *Percentage change of cord length, SPADI and Fact-B scores after physiotherapy. L=left, R=right.*

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	68,16	79,04	**+16**
SPADI (pain)	33	4	**-87.9**
SPADI (disability)	45	13	**-71.1**
SPADI (total)	78	17	**-78.2**
FACT-B (physical)	20	9	**-55**
FACT-B (social)	28	25	**-10.7**
FACT-B (emotional)	13	12	**-7,7**
FACT-B (functional)	22	22	**0**
FACT-B (additional concerns)	15	14	**-6.7**
FACT-B (total)	98	81,5	**-16.8**

All movements on both arms improved or stayed the same after physiotherapy, except for a minimal change in internal rotation in the unaffected arm (Figure 7.21). The biggest improvements were on internal rotation of the affected arm with a 500% increase post-physiotherapy, abduction with 38.3% increase and forward flexion with 28.3% increase. The improvements mimicked the reduced difficulty she had in washing her hair and back.

There was also a reduction in the difference between the two arms except for forward flexion, even though both arms improved. Abduction and forward flexion were not at full range of motion (Clarkson & Gilewich, 1989), which might be related to the persistence of the cord. However, improved ROM seemed to be associated with reduced pain and disability scores.

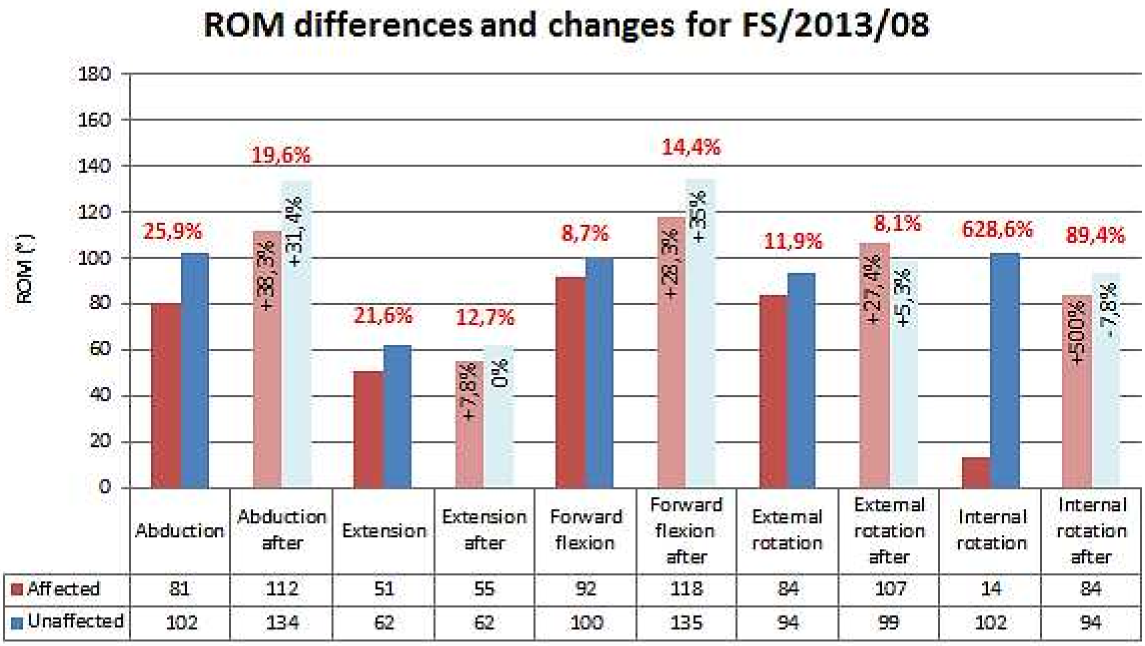

Figure 7.21. *The difference between left and right arms and improvement on range of movements for patient FS/2013/08 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*

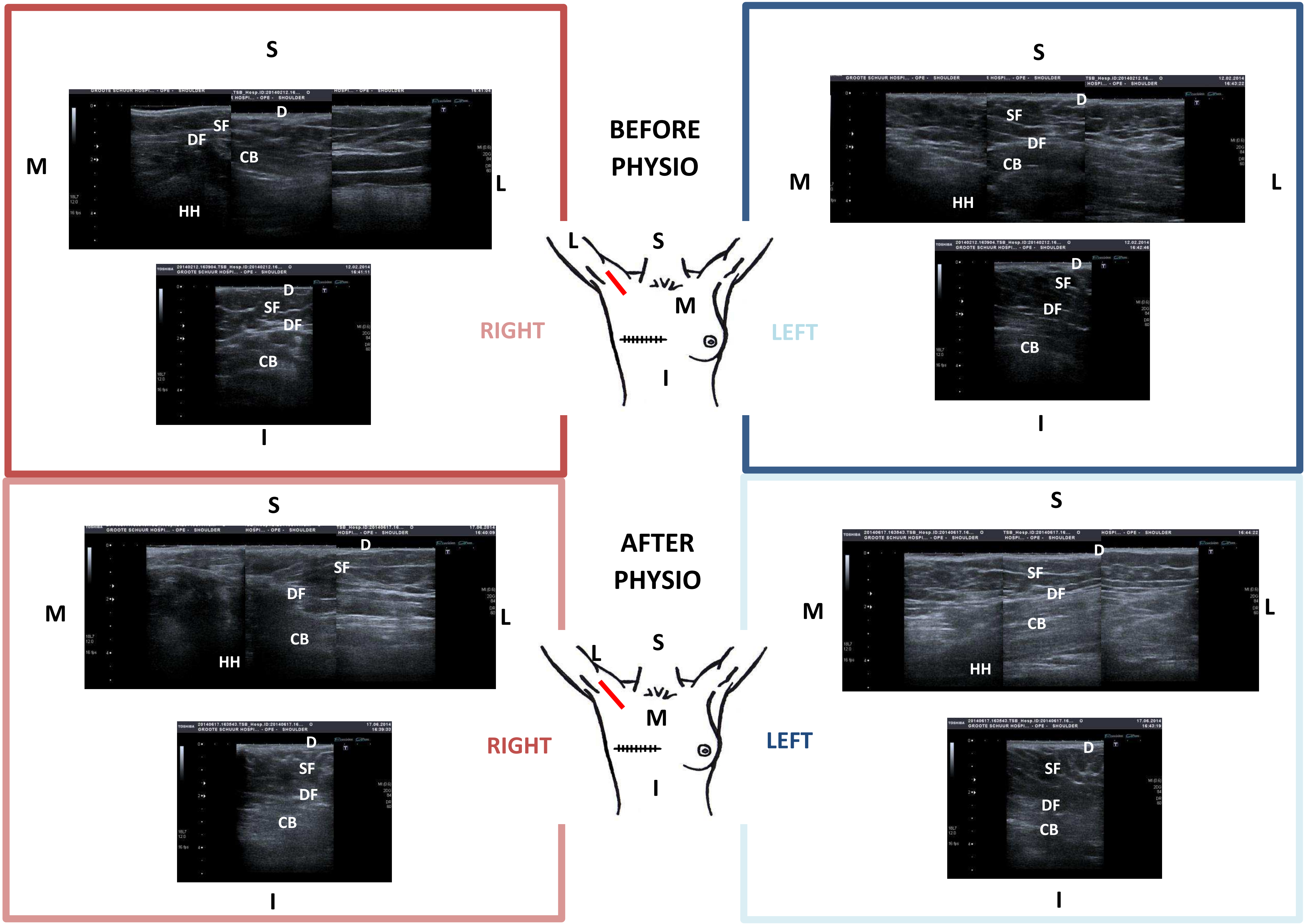

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Plate 7.8.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/08 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.8.4. Ultrasonography Plate 8

7.8.4.1. Static

7.8.4.1.1. Left

On the left longitudinal ultrasound scans there was an approximate 1.5-2 cm adipose tissue layer within regular, continuous strands of superficial fascia (SF) forming a honeycomb structure. The deep fascia (DF) was intact over the coracobrachialis muscle (CB) which showed its epimysial layers, although not very clearly, within it. On the transverse scan there appeared a similar organisation with clear fascial bands visible through the tissues. Post-physiotherapy there was increased contrast showing similar organisation but better definition of the structures.

7.8.4.1.2. Right

On the right longitudinal scans there seemed to be greater disruption in the superficial fascial layers with increased thickening at the dermal-hypodermal junction, strong connections between the SF and the dermis (D) and more coarse homogeneity throughout. On the transverse scan the SF showed slightly thickened with the DF forming a fibrous scar. After physiotherapy the disorganisation was still visible with thickened fascial planes but with slightly more regularity and less connection to the skin.

7.8.4.2. Dynamic

On the ultrasound videos there was slightly more regularity and less thickening of the superficial fascia and dermis on the unaffected arm (Video 8.1) compared to the affected arm (Video 8.3). After physiotherapy the abovementioned differences between affected and unaffected arms were shown again on Videos 8.2 and Video 8.4, but no other clear differences were detected.

7.8.4.3. Links between outcome measures

Although the cord remained visible on the surface, there were some fascial changes that could possibly be related to the ROM and pain improvements and differences. The fascial planes-were less adhesive post-physiotherapy, although there was still thickening of the fascia close to the dermis on the affected side, possibly relating to the residual cord.

7.9. Patient FS/2013/09

Table 7.17. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	53 years	
Side affected	Left	
Handedness	Right	
Treatments	**Surgery**	Left mastectomy + left ANC
	Chemotherapy	CAF (x6)
	Radiotherapy	47 Gy (2.67 Gy/frac) chest wall, medial and superior half axilla of axilla, supraclavicular area
	Hormonal therapy	Tamoxifen
No. of days surgery until presentation	1122 days	
Self-reported symptoms before	Pain, cording and limited range of movement	
Drop-out	Cord resolution but socioeconomic and personal problems prevented her from continuing the study	

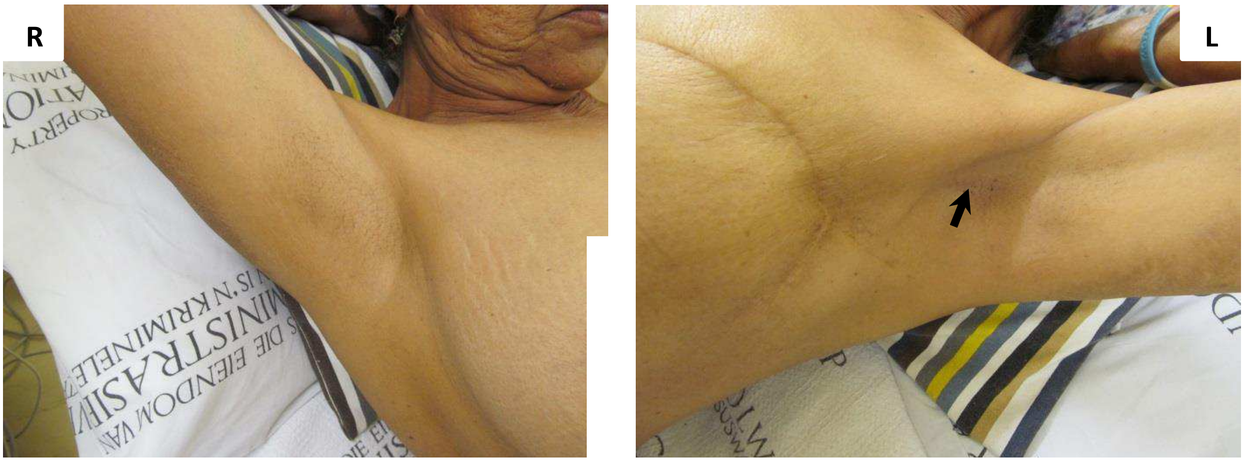


Figure 7.22. *With the arm in the ABER position, showing the cord (arrow) for patient FS/2013/09. L=left, R=right.*

7.9.1 Patient description

A 53-year-old patient presented 1122 days after surgery with pain, cording and tightness in the axilla and limited range of movement (Table 7.17, Figure 7.22).

The patient was treated with a left mastectomy and axillary node clearance for breast carcinoma. She received neoadjuvant six courses of CAF chemotherapy and started with Tamoxifen soon after her surgery. Two years later she received 47 Gy adjuvant radiotherapy to the chest wall, medial and superior half axilla of axilla and supraclavicular area (2.67 Gy/frac), approximately a year before she entered the study.

Although the physiotherapist examined her and no clear cord was observed, she could not continue with the study due to personal problems.

7.9.2. Surface anatomy

Figure 7.22 shows a taut band of tissue on the left arm that retracted the skin inwards within the axillary vessel groove between coracobrachialis and teres major and latissimus dorsi muscles. The cord started in the middle of the axilla and extended towards the lateral side of the upper limb.

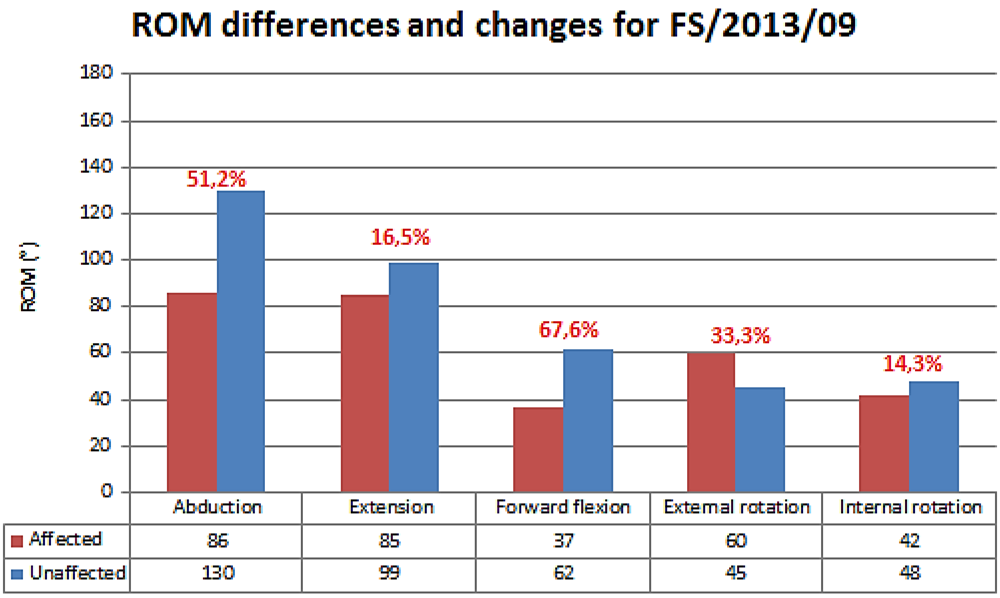
7.9.3. Measurements

At the first measurement cycle the cord measured approximately 58.08 mm in length (Table 7.18). The patient reported a high amount of pain (41/50) but a moderate amount of disability (56/80) when prompted with the SPADI questions. She experienced a lot of pain when 'reaching high' (10/10) or when 'lying on the involved side' (9/10) and could not by herself 'put an object on a high shelf', 'carry a heavy object' or 'wash her hair or back' with the affected arm (10/10). All her FACT-B scores were lower, giving a low total score of 77.2/144, indicating a low quality of life exacerbated by the pain and disability.

Table 7.18. *The different scores for the outcome measures of cord length, SPADI and FACT-B.*

Values at first measurement cycle	
Outcome measure	**Before**
Cord length (mm)	58.08
SPADI (pain)	41
SPADI (disability)	56
SPADI (total)	97
FACT-B (physical)	15
FACT-B (social)	15
FACT-B (emotional)	20
FACT-B (functional)	17
FACT-B (additional concerns)	10
FACT-B (total)	77.2

All ROM measures, except external rotation, on the affected side were lower than on the unaffected side (Figure 7.23). The external rotation measure could be explained as being due to her right handedness. The patient's most affected actions were abduction and forward flexion with a 51.2% and 67.6% difference, respectively, between the lower and the higher scores. The reduced actions in her affected arm correlated with the tightness in her axilla preventing her from reaching high (forward flexion) or washing her hair (abduction).



	Abduction	Extension	Forward flexion	External rotation	Internal rotation
Affected	86	85	37	60	42
Unaffected	130	99	62	45	48

Figure 7.23. *The difference between left and right arms on range of movements for patient FS/2013/09. The left side is highlighted in blue and the right side in red. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference.*

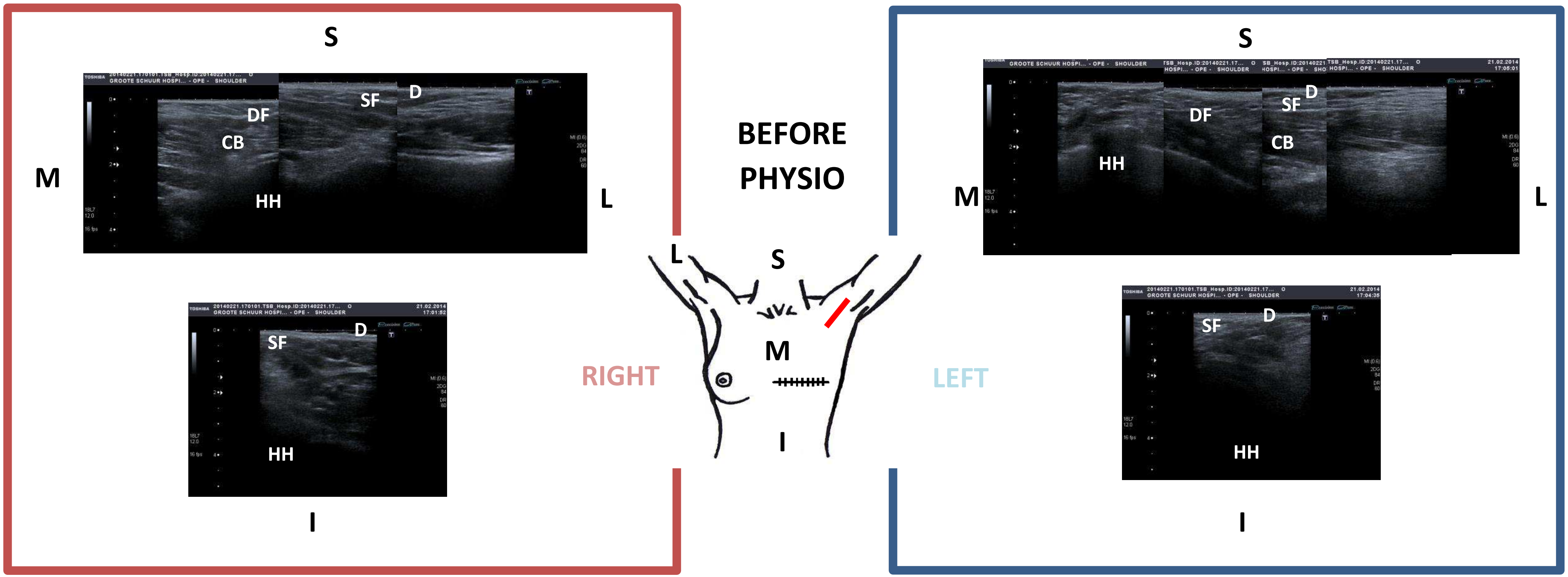

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Plate 7.9.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/09 before physiotherapy as indicated by the torso pictogram. The torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.9.4. Ultrasonography Plate 9

7.9.4.1. Static

7.9.4.1.1. Left

On the affected side on the longitudinal scans there was approximately 1 cm of adipose tissue present. Within the hypodermis the superficial fascia (SF) was multi-layered and more densely packed on the far-most right image but more disrupted and thicker on the left, closer towards the area below the scar superficially. There were some shadowy artefacts within the muscle (CB). The unclear continuity was also visible on the transverse scan which had a coarse homogeneity and some hypoechoic shadows, probably from vessel lumen. On both the transverse and longitudinal scans the superficial fascia showed connections to the skin, but was more visible on the transverse ultrasonograph.

7.9.4.1.2. Right

On the right unaffected side, the hypodermal thickness was slightly less (0.5-1 cm) but the SF was showing more regular throughout, was more organised and more obvious surrounding the vasculature on the transverse scan. The deep fascia (DF) also seemed slightly thicker on the unaffected side, compared to the affected side.

7.9.4.2. Dynamic

On Video 9.1 of the left side there appeared to be more disrupted SF strands extending from the skin to the DF and muscle. On Video 9.2 independent muscle gliding was present and continuity and linearity of the SF fibres in the hypodermis was more obvious than in Video 9.1. The videos are, however, not very clear.

7.9.4.3. Links between outcome measures

Although there was a fibrous band and tightness in the axilla, no clear cord was observed by the physiotherapist or on the ultrasound scans. There were, however, close skin connections and less regularity found in the superficial fascia layers of the affected arm compared to the unaffected arm. The findings correlated with the tightness on the surface and could be associated with the low SPADI and FACT-B scores as experienced by the patient due to pain, discomfort and limited shoulder movement.

7.10. Patient FS/2013/10

Table 7.19. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	48 years	
Side affected	Left	
Handedness	Right	
Treatments	**Surgery**	left mastectomy + left ANC
	Chemotherapy	CAF (x6)
	Radiotherapy	42.7 Gy (2.67 Gy/frac) chest wall, medial and superior half axilla of axilla, supraclavicular area
	Hormonal therapy	Tamoxifen + Arimidex
No. of days surgery until presentation	1133 days	
Self-reported symptoms before	Cord, pain and limited range of movement	
Drop-out	Did not respond to calls to come for physiotherapy	

Figure 7.24. *With the arm in the ABER position, showing the cord (arrow) for patient FS/2013/10 with the arm in the ABER position. L=left, R=right.*

7.10.1. Patient description

A 48-year-old woman presented 1 133 days post-surgery with a clear cord on the left side, puckering around the scar, pain and restriction upon movement of the arm and shoulder (Table 7.19, Figure 7.24).

The patient was treated with a left breast mastectomy and axillary node clearance for breast carcinoma. She received adjuvant six courses of CAF, was prescribed Tamoxifen and after that

Arimidex and received 42.7 Gy radiotherapy to the chest wall, medial and superior half axilla of axilla and supraclavicular area (2.67 Gy/frac).

Although the patient expressed interest in being part of the study, the physiotherapist was unable to make an appointment with her for treatment after the first measurement cycle.

7.10.2. Surface anatomy

A clear double finger-thick cord was observed in the mid-axillary line extending inferiorly from the scar-line fanning superiorly towards the lateral upper arm (Figure 7.24). Clear puckering was noticed around the scar as well as around the root of the cord, showing slight retraction of the skin.

7.10.3. Measurements

At the first measurement cycle the cord measured 91.34 mm across the axilla (Table 7.20) which restricted some movements and caused pain. The patient, for example, reported increased pain 'reaching high' (10/10) or 'pushing with the involved arm' (10/10) and disability when 'putting an object on a high shelf' (10/10) or 'washing her back' (7/10), but little other difficulty as reflected in her SPADI scores (71/130). The patient's FACT-B scores mirrored the item scores as she had a high quality of life score of 124.5/144.

Table 7.20. *The different scores for the outcome measures of cord length, SPADI and FACT-B.*

Values at first measurement cycle	
Outcome measure	**Before**
Cord length (mm)	91.34
SPADI (pain)	26
SPADI (disability)	45
SPADI (total)	71
FACT-B (physical)	21
FACT-B (social)	25
FACT-B (emotional)	20
FACT-B (functional)	27
FACT-B (additional concerns)	32
FACT-B (total)	124.5

The action that was most debilitated was abduction with the unaffected arm having a 133.8% higher ROM measure (Figure 7.25). Internal rotation showed a 56.9% difference between the unaffected and affected arms and forward flexion was affected on both sides but showing a 18.9% higher score on the unaffected arm. Her disability in reaching high, putting something on a high shelf and washing her back reflected in the scores.

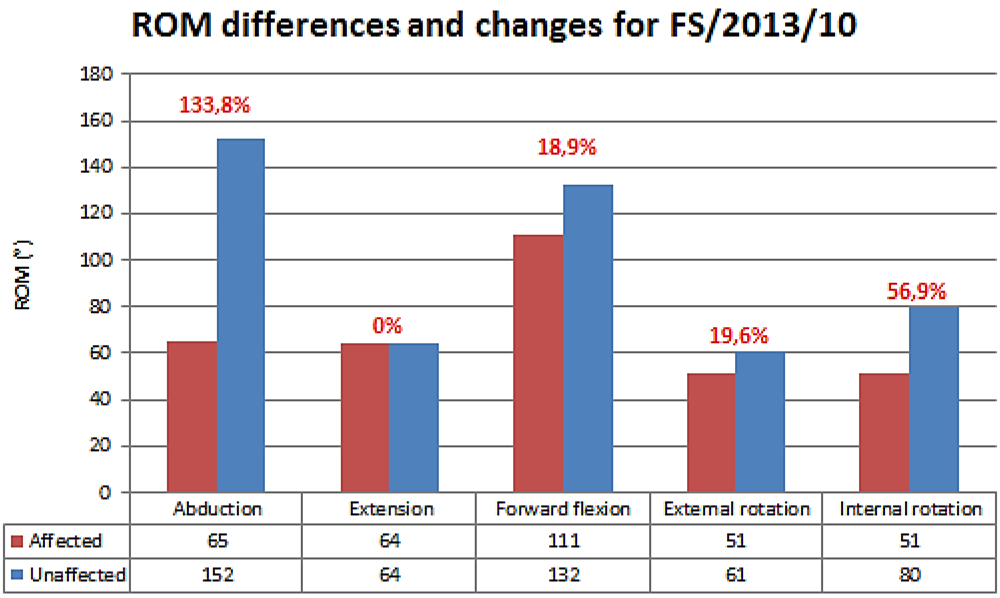

Figure 7.25. *The difference between left and right arms on range of movements for patient FS/2013/10. The left side is highlighted in blue and the right side in red. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference.*

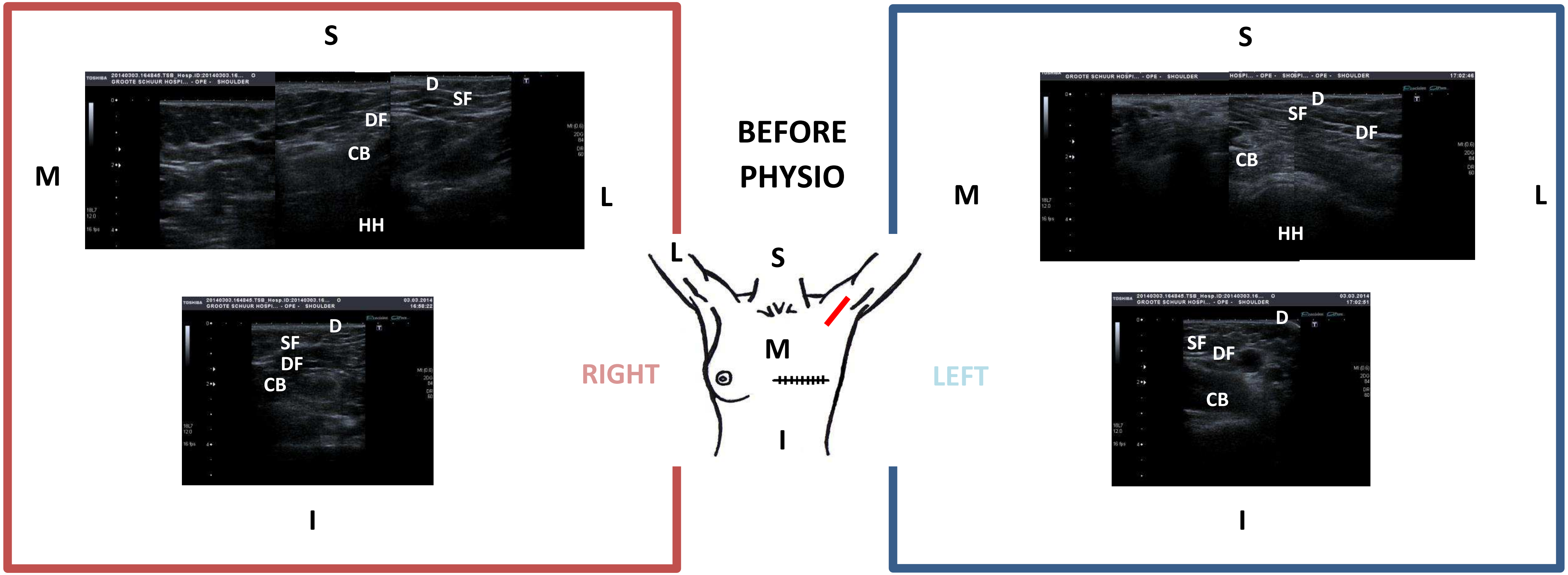
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Plate 7.10.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/10 before physiotherapy as indicated by the torso pictogram. The torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head

7.10.4. Ultrasonography Plate 10

7.10.4.1. Static

7.10.4.1.1. Left

On the longitudinal scans of the left affected side there was approximately 1-1.5 cm of adipose tissue. Within the adipose tissue there was scarce, thickened superficial fascia which had a diffuseness surrounding it and disappeared in an area of high coarse homogeneity on the left of the images. The coarseness was spread throughout the hypodermis and coracobrachialis muscle (CB). A shadowy artefact appeared near the CB marker. The superficial fascia seemed closely associated with the skin with which it connected on multiple points. On the transverse ultrasound scan the organisation of the SF was not regular, thinner and surrounded a hypoechoic lumen.

7.10.4.1.2. Right

On the right the adipose tissue was 1.5-2 cm with honeycomb-like organised superficial fascia throughout it. The deep fascia (DF) was unclearly defined on the ultrasound scan but appeared continuous over the CB, which itself appeared diffuse as well - possibly relating to a scanning artefact. On the transverse scan the SF appeared more linear and regular compared to the left but was not very clear.

7.10.4.2. Dynamic

There appeared more continuity and organisation and slightly better muscle gliding on the unaffected side (Video 10.2, Figure 7.26 (R)) compared to the affected side (Video 10.1, Figure 7.26 (L)) Furthermore, the superficial fascia was very closely connected to the dermis on the affected side (Figure 7.26 (L)).

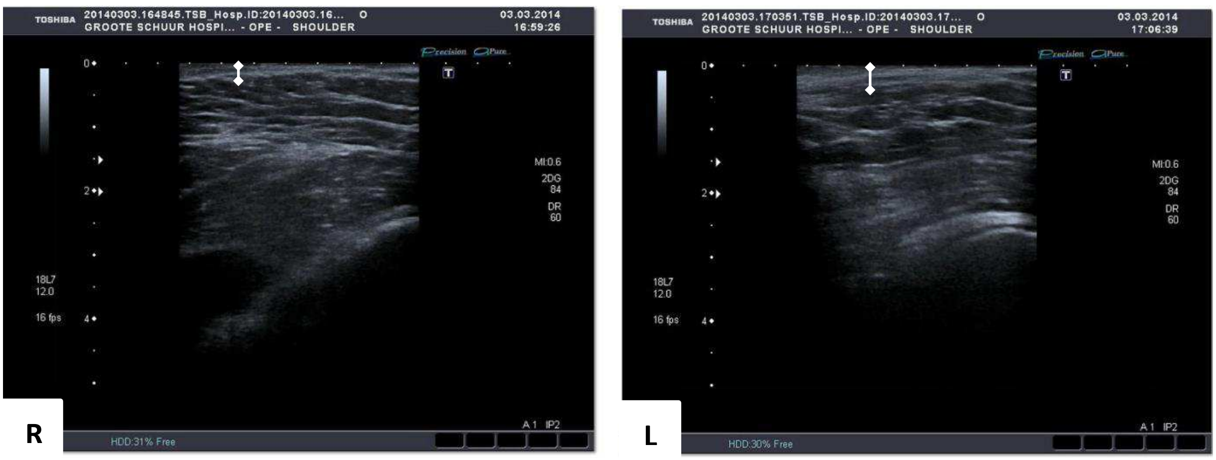


Figure 7.26. *Video stills showing the difference in relationship of the superficial fascia to the dermis, being thicker and more closely connected on the ultrasound scans of the affected (left) compared to the unaffected (right). L=left, R=right.*

7.10.4.3 Links between outcome measures

Although the patient had an obvious long and thick cord on the surface, which seemed to cause some pain and discomfort with particular movements and actions, a clear cord structure was not visible on the ultrasound scans. The puckering and close relationship of the SF with the dermis could explain the puckering and tightness, and perhaps the cord itself was obscured by the dense connective tissue in the hypodermis.

7.11. Patient FS/2013/11

Table 7.21. *Participant variables describing age, affected side, handedness and treatment details.*

Patient details		
Age	51 years	
Side affected	Left	
Handedness	Right	
Treatments	**Surgery**	Left mastectomy + left ANC
	Chemotherapy	CAF (x6)
	Radiotherapy	42,7 Gy (2,67 Gy/frac) chest wall + medial axilla
	Hormonal therapy	Tamoxifen
No. of days surgery until presentation	601 days	
Self-reported symptoms before	Cording	
Self-reported symptoms after	Cording	
No. of physiotherapy treatments	5	
Physiotherapy focus	Tightness in scar; myofascial release of scar and fat pad in axilla	

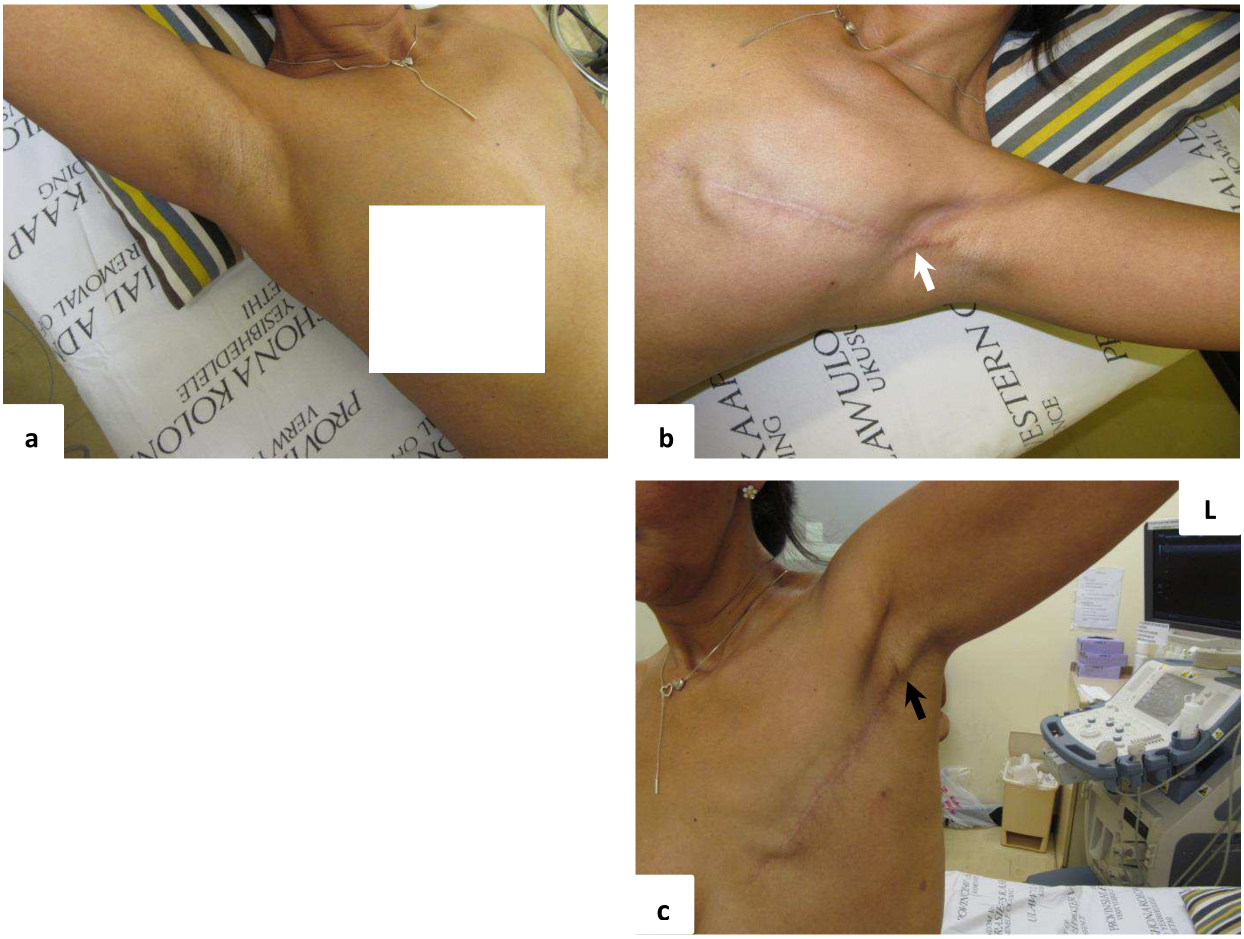


Figure 7.27. *With the arm in the ABER position, showing the cord (arrow) and scar area on the left side for patient FS/2013/11 before physiotherapy with the arm in the ABER position (a) compared to the right (b) and the patient standing with arm in abduction (c). On (c) a clear thickening is visible in the mid-axilla. L=left, R=right.*

7.11.1. Patient description

A 51-year-old patient presented 601 days post-surgery with a complaint of tightness and cording in the left axilla (Table 7.21, Figure 7.27).

The patient was treated with a left breast mastectomy and left axillary node clearance for breast carcinoma. She received neoadjuvant six courses of the CAF regimen and adjuvant Tamoxifen and 42,7 Gy radiotherapy to the chest wall and medial axilla (2,67 Gy/frac).

The physiotherapist noted a palpable but not tender lump mid-axilla – which was visible on Figure 7.27a. There was no puckering or excess tissue but slight adherence to the chest wall. Physiotherapy treatment was focused on the myofascial release of the cord, the lump in the axilla and the chest wall tightness and pectoralis major and minor, latissimus dorsi and the scapular muscles.

As a result of an interest in comparing the cord on US and MRI, patient 11 was selected to undergo an MRI scan before undergoing physiotherapy treatment (Figure 7.28b), which was included in the study.

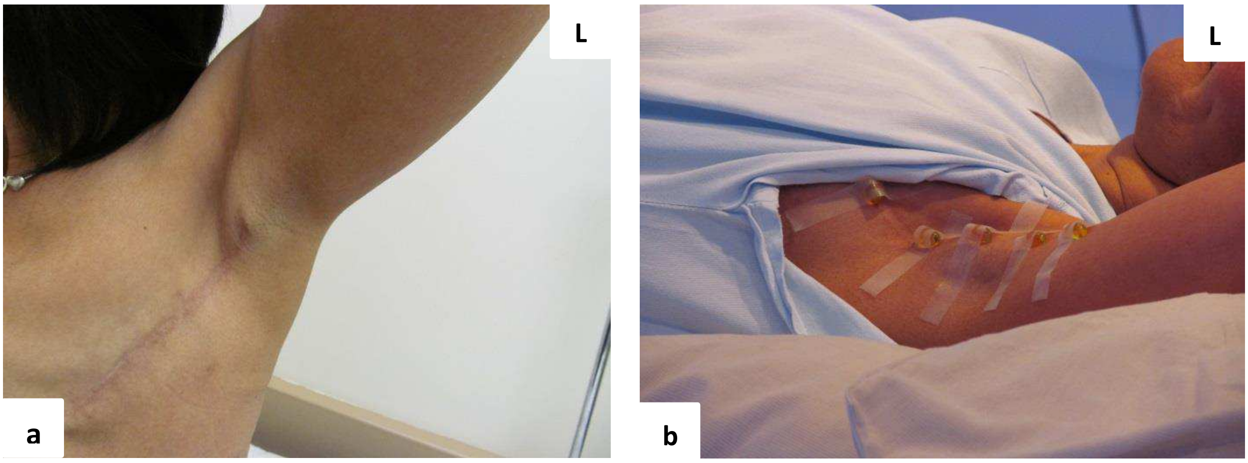


Figure 7.28. *With the arm in abduction, showing the cord and scar area for patient FS/2013/11 at the time of the MRI scan. (a) - shows the cord similar to Figure 4.56c - and in the ABER position (b) shows the beads that are put on the cord area for the MRI scan. L=left, R=right.*

7.11.2. Surface anatomy

A web of guitar string-like cords presented in the unusual lower aspect of the axilla in the axillary vessel groove, extending from the inferior portion of the scar line to the middle of the axilla. The first cord was visible in Figure 7.27, whereas the second cord was not visible on the photographs. A lump was visible over the cord (Figure 7.27c) when the patient was standing upright.

After physiotherapy the cord partly resolved showing a slight remnant of the structure still visible in the axilla (Figure 7.29).

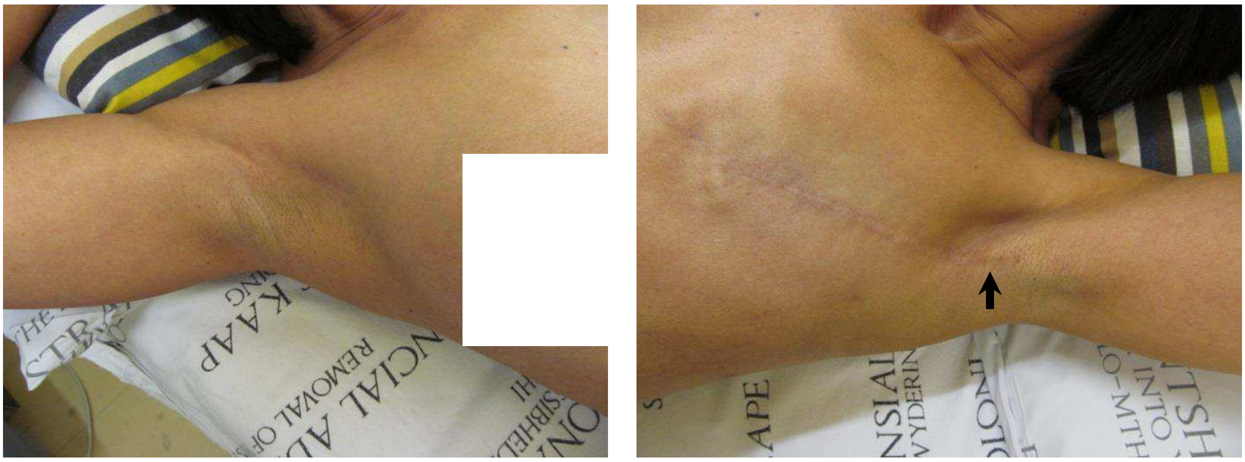


Figure 7.29. *With the arm in the ABER position, showing the cord and scar area for patient FS/2013/11 after physiotherapy with the arm in the ABER position. L=left, R=right.*

7.11.3. Measurements

At the first measurement cycle the cords measured 139.52 mm and 57,96 mm. After physiotherapy, the second cord resolved completely, whereas the first cord reduced by 30.3% in length to 97, 19 mm (Table 7.22).

Although the patient had some tightness in the axilla, she did not experience a lot of pain but some pain when 'lying on the involved side' (4/10) or 'reaching high' (5/10) and had some difficulty with 'putting an object on a high shelf' (3/10) or 'washing her hair' (3/10). The item scores mirror what the physiotherapist found as the only areas the patient had difficulty with were the abovementioned, otherwise she could manage all the activities of daily living. Her SPADI scores corroborated that finding with relatively low scores for pain and disability (14/50 and 8/80) which decreased even further to no pain and little disability (4/80) when placing objects high up, after physiotherapy.

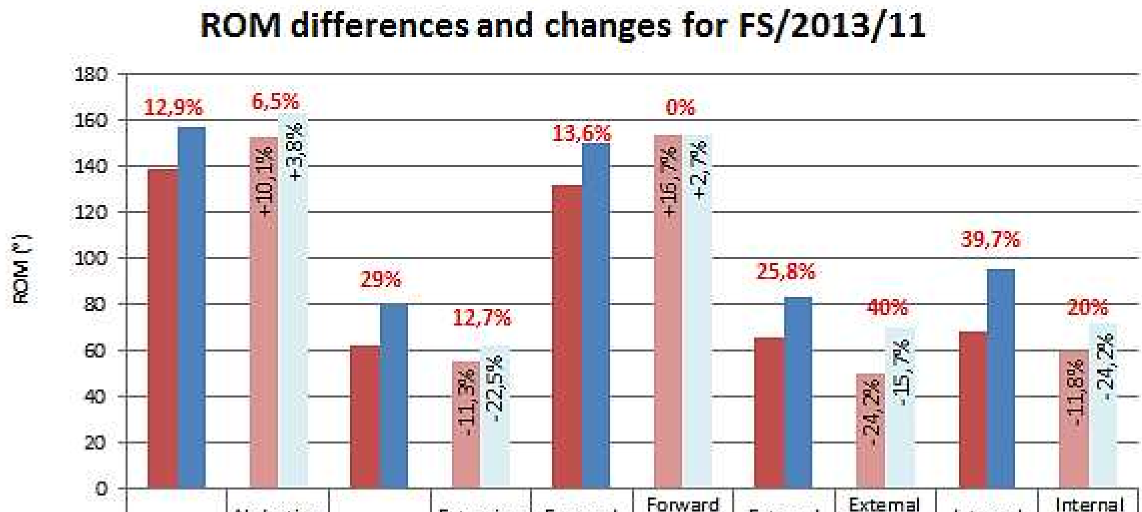
The abovementioned low scores for pain and disability were reflected in the Fact-B score where the patient's score improved but her initial score was higher, showing only a small 4,1% improvement overall. She had some anxiousness regarding the disease progression in the emotional subsection which improved after physiotherapy but otherwise the patient had no physical problems before or after physiotherapy.

Table 7.22. Percentage change of cord length, SPADI and FACT-B scores after physiotherapy.

Changes after physiotherapy			
Outcome measure	**Before**	**After**	**Change (%)**
Cord length (mm)	139.52 (57.96)	97.19	**-30.3 (-100)**
SPADI (pain)	14	0	**-100**
SPADI (disability)	8	4	**-50**
SPADI (total)	22	4	**-81.8**
FACT-B (physical)	24	27	**+12.5**
FACT-B (social)	28	26	**-7.7**
FACT-B (emotional)	14	15	**+7.1**
FACT-B (functional)	27	26	**-3.7**
FACTFACT-B (additional concerns)	21	25	**+19**
Fact-B (total)	114	118.7	**+4.1**

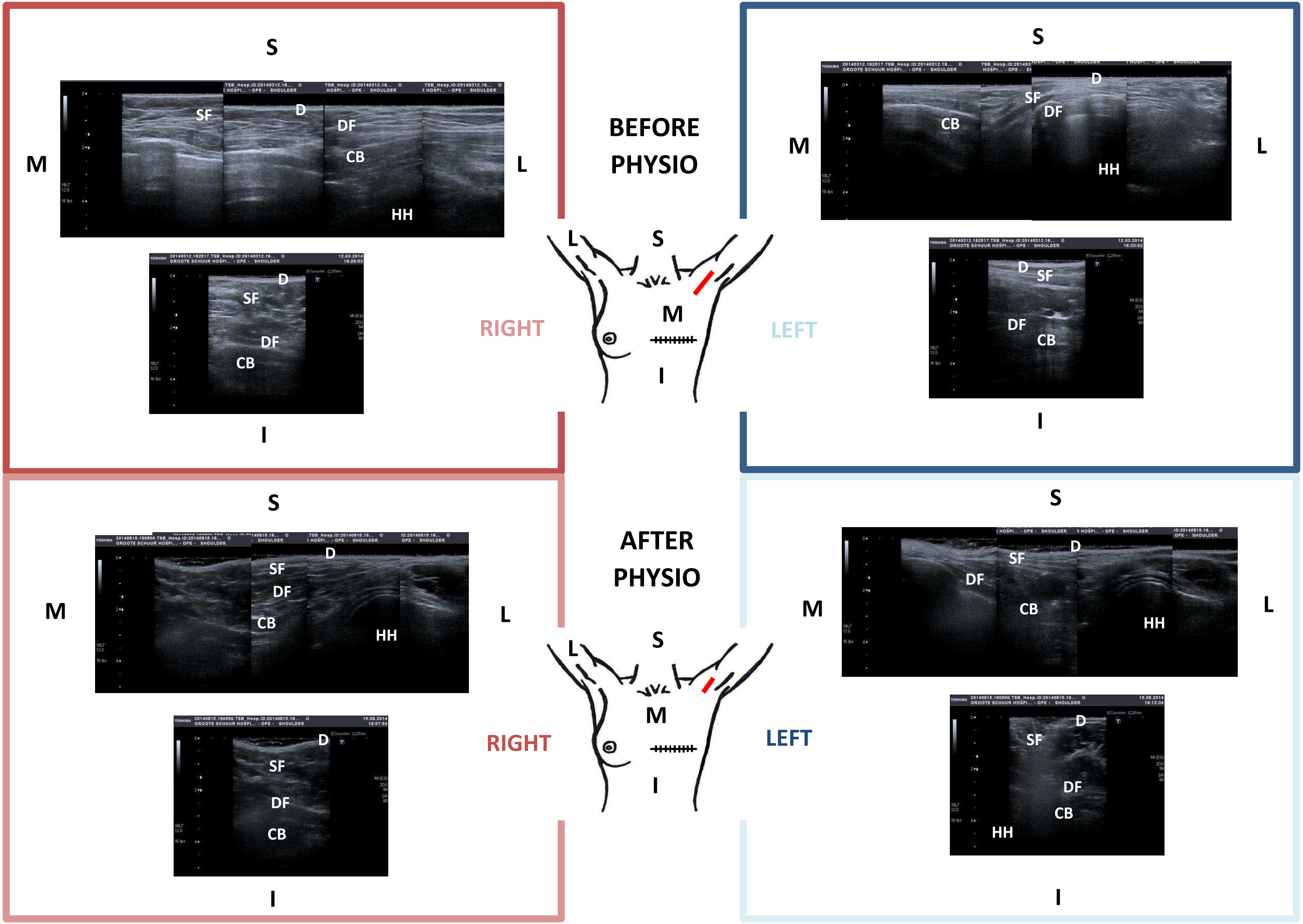
The patient's range of movement showed very little improvement, being 16.7% in forward flexion and 10.1% in abduction of the affected arms (Figure 7.30). Both unaffected arms seemed to improve for the actions as well and showed less difference between the arms after physiotherapy. The reduced difference between arms mirrored the results from the SPADI scores where there was improvement in functioning due to less pain and disability being experienced.

Extension, external and internal rotation showed a decrease of up to 24% on both arms after physiotherapy but still remained in normal range of motion (Clarkson & Gilewich, 1989).



	Abduction	Abduction after	Extension	Extension after	Forward flexion	Forward flexion after	External rotation	External rotation after	Internal rotation	Internal rotation after
Affected	139	153	62	55	132	154	66	50	68	60
Unaffected	157	163	80	62	150	154	83	70	95	72

***Figure 7.30.** The difference between left and right arms and improvement on range of movements for patient FS/2013/11 after physiotherapy. The left side is highlighted in blue and the right side in red, with both lighter colours depicting the ROM after physiotherapy. The red bolded percentage indicates the percentage difference between left and right with the lowest value being the reference. The percentages inside the after bars indicate the percentage change (+/-) with respect to the before value.*


BEFORE PHYSIO
AFTER PHYSIO
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HH

Plate 7.11.

Overview of ultrasound scans of the cord in the axillary region of patient FS/2013/11 before (top) and after (bottom) physiotherapy as indicated by the torso pictograms. Each torso pictogram denotes the position and an indication of the length of the cord in red. The ultrasound scans for each side were placed at the side of the pictogram with the longitudinal scans at the top and the transverse scans at the bottom. The longitudinal scans are aligned along the cord length; the transverse scan taken mid-cord. Orientation indicators: S=superior, I=inferior, L=lateral, M=medial. Within the scans: D=dermis, SF=superficial fascia, DF=deep fascia, CB=coracobrachialis muscle, HH=humeral head.

7.11.4. Ultrasonography Plate 11

7.11.4.1. Static

7.11.4.1.1. Left

On the left longitudinal ultrasound scan there was an adipose tissue layer of approximately 0.5-1 cm thickness present. Within the adipose tissue there was increased coarse homogeneity and a thickened superficial fascia (SF) present that was partly continuous. Numerous broken fibrous thinner strands with an increased connection to the dermis were shown with a particular densified patch close to the dermis (D) demarcation. The coracobrachialis (CB) muscle and its fascia (DF) was not very clearly as shown on the scan. On the transverse scan the SF appeared thickened again. Post-physiotherapy, there seemed to be more regularity of the SF and multi-layering, with more space between the individual strands, and reduced coarse homogeneity. The transverse scan showed an artefact and the focal thickening of the SF was still present.

7.11.4.1.2. Right

On the right longitudinal scans there was a clearly defined multi-layered and regular SF that connected to the DF and D. There seemed to be more regularity in the CB with more perpendicular epimysial fascia layers present. The transverse scan showed a latticework organisation for vessels and nerves. Post-physiotherapy the layering was somewhat less clear on the ultrasound scans but was still multi-layered and structurally organised as before. Similarly, the transverse scan showed the honeycomb organisation as pre-physiotherapy and more organised on the right than on the left.

7.11.4.2. Dynamic

On the affected side on Video 11.1 there was increased thickness of the superficial fascial bands which were more disrupted compared to the more continuous planes in Video 11.3 on the unaffected side and more connected to the D. Post-physiotherapy increased muscle gliding on both scans was visible, but the disrupted superficial fascial layers were still evident on the affected side on Video 11.2 compared to the unaffected side on Video 11.4.

7.11.4.3. Links between outcome measures

Although the cord did not resolve fully, the improvements in both range of movement and pain showed as slight fascial reorganisation on the ultrasound scans. Increased multilayering of the superficial fascia, decreased connectivity to dermis and more independent tissue gliding appeared after the physiotherapy treatment, all of which can be associated with the reduced tightness in the axilla and on the chest wall and freer ROM.

7.11.4.4. MRI

On the MRI scan it was noted that the axillary swelling was composed of multiple linear fibrotic bands superiorly that confluenced with the subcutaneous adipose tissue of the upper arm and axilla to become a fibrotic cord (Figure 7.31, red arrows).

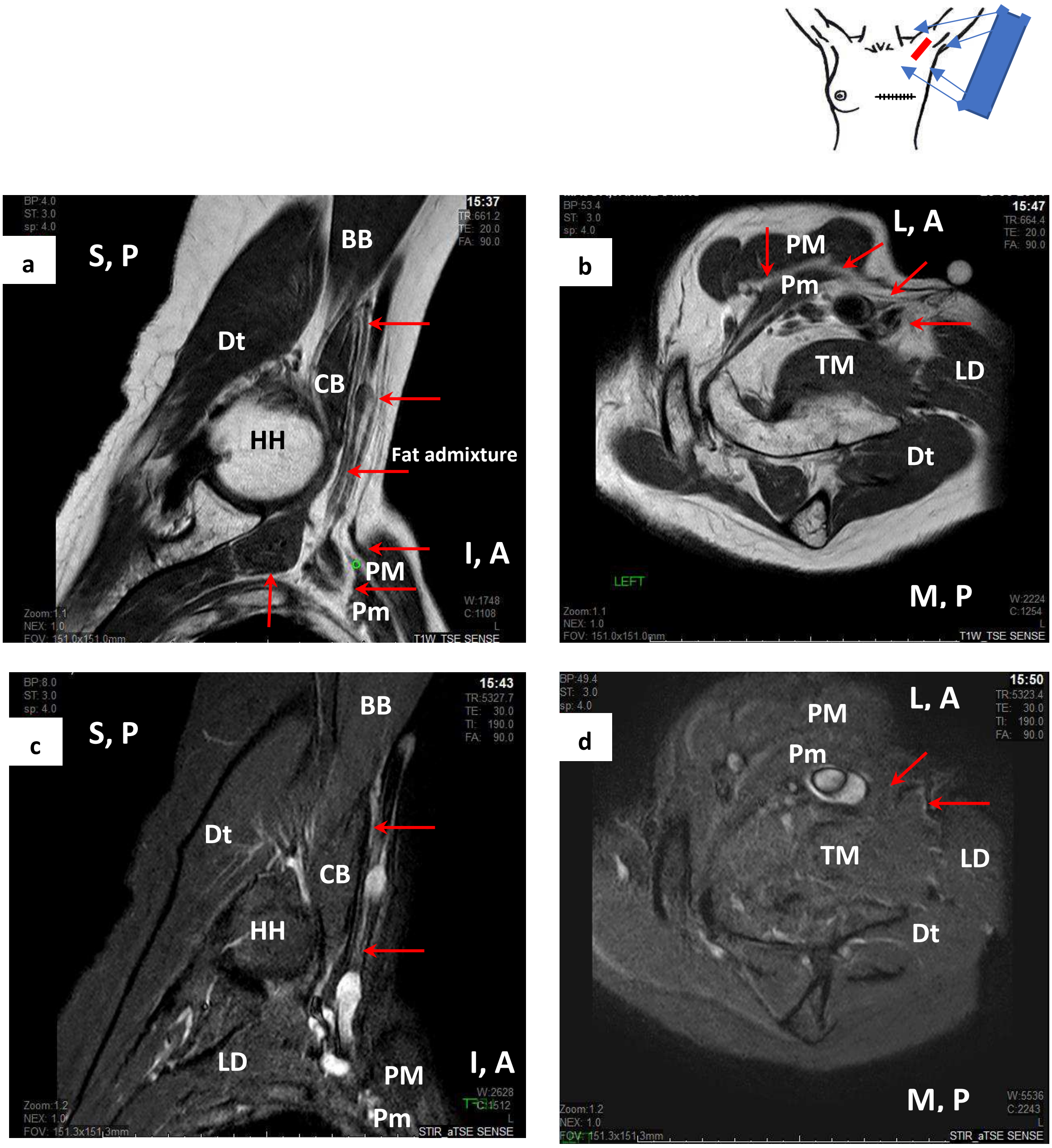


Figure 7.31. *Long axis STIR PDFS T1 (a and b) and short axis STIR T1 (c and d) MRI images of the arm in the ABER position as shown in Figure 4.57b. Figures a and c are in parasaggital view; b and d in axial view. The red arrows indicate the fibrous bands. For orientation, the torso pictogram is placed at the top, indicating the direction of the unconventional MRI scanning of the cord (red line). Orientation indicators: S=superior, I=inferior, P=posterior, A=anterior, L=lateral, M=medial. Within the scans: HH=humeral head, BB=biceps brachii, Dt=deltoid, CB=coracobrachialis, TM=teres major, LD=latissimus dorsi, PM=pectoralis major, Pm=pectoralis minor.*

The multiple thin fibrous bands at the site of the axillary web extended into the hypodermis at the junction of the upper arm and axilla. The bands lay superficial to the skin and had short axis dimensions of 2.6 x 8.2 mm with the whole fibrotic area measuring 6.5 cm. The fibrous tissue showed low signal on all the sequences.

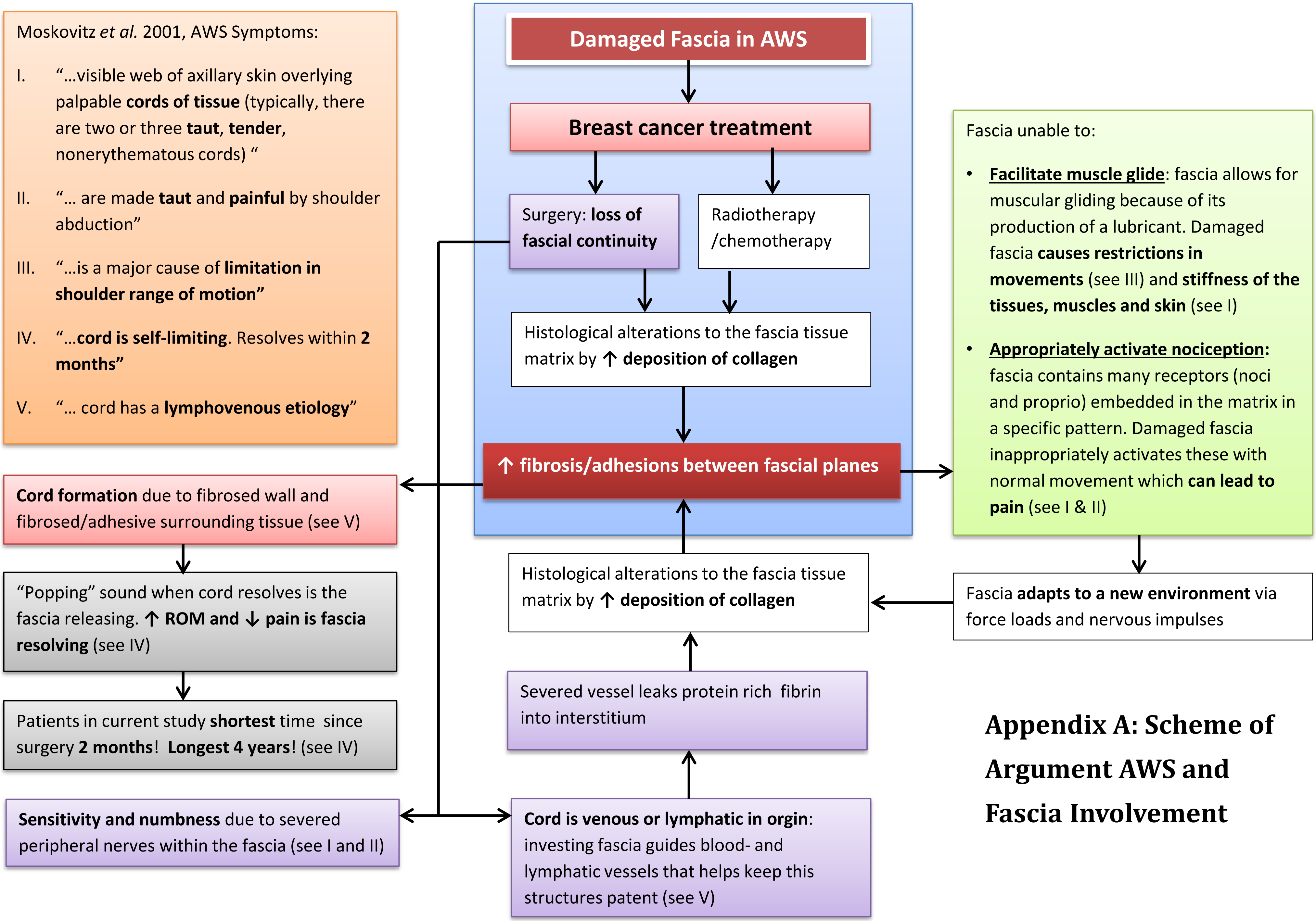
There was also prominent adipose tissue mixed with the fibrotic bands which accounted for the larger swelling evident clinically (Figure 7.31, see label fat admixture). No STIR hyperintensity within the bands or conglomerate cord indicated a vascular or lymphatic contribution.

A distal clear fibrous band connected the conglomerate cord to the pectoralis major muscle postero-caudally (PM). A lesser band originated from the pectoralis minor (Pm) muscles and merged with the axillary cord. Proximally, inferiorly on the image, the cord continued to become inseparable with the anterior border of latissimus dorsi (LD) and its fascia. The most inferior extent of the lesion was not included.

7.11.4.5. Links between ultrasound, MRI and outcome measures

There were several agreements between our ultrasound and MRI finds which included an increased thickness of the multi-layered dense superficial fascia which had increased connection with the dermis and some musculature, which explained some difficulty in movement, and pain upon movement, which prevented independent muscle gliding.

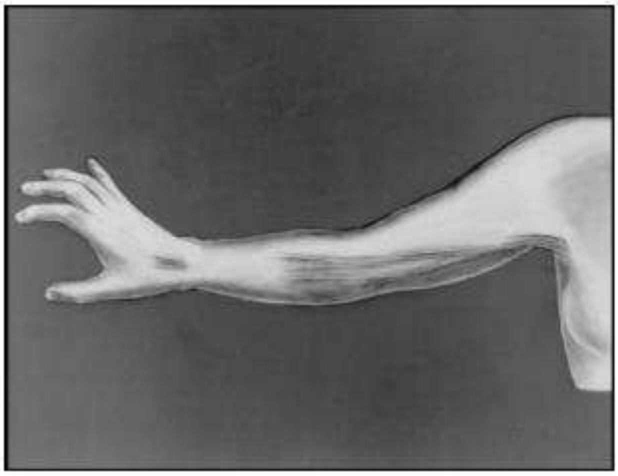
APPENDICES



Appendix A: Scheme of Argument AWS and Fascia Involvement

Appendix B: Participant Information, Reply Slip and Consent Form

Participant Information Leaflet



Adapted from Moskovitz et al. (2001).

Date: 04-06-2013 Version: 01

TITLE OF THE RESEARCH PROJECT: Axillary Web Syndrome (AWS) after treatment for breast cancer: comparing clinical variables with ultrasound imaging data focussing on anatomical changes before, during and after physiotherapy treatment.

PRINCIPAL INVESTIGATOR:	Dr Delva Shamley	021 406 6281
CO-INVESTIGATORS:	Dr Charles Slater	
	Mr Willie Fourie	
	Dr Hannah Simonds	021 404 4267
	Mr Kyle Paulssen	079 091 6904

ADDRESS: Department of Human Biology, Level 2, Anatomy Building, Faculty of Health Sciences, University of Cape Town, Observatory, 7925

Invitation to participate: We are inviting you to take part in a research project in breast cancer because you have been treated for breast cancer in the past. The information in this letter explains the details of the project and how you could be involved. Please ask your doctor to explain anything that you do not understand. Only you can decide if you want to take part and, if you choose to say no or to withdraw from the study at any time, it will not affect your medical treatment in any way, not now or in the future.

What is the study about? Axillary web syndrome (AWS) is a disorder which may develop as a side effect of the treatment for breast cancer. It is characterised by a tight cord that runs over the inside of the arm from the armpit and can extend to the thumb. This cord will tighten and become more visible when lifting the arm, which can be painful and difficult. Not all women treated for breast cancer develop the complications and we do not know why some women have problems and others do not.

This study will be the one of the first that looks at how a cord responds to physiotherapy treatment. We would like to do this by viewing the cord before, during and after treatment using ultrasound images of your arm and shoulder. We hope this will assist us to learn more about the disorder and develop better treatment for patients like you.

Ethical approval: This study has been approved by the University of Cape Town Human Research Ethics Committee which promotes respect for the research participants and protects their health and their rights.

Who will be doing the research? All of the researchers and health professionals who will be involved are experts in their field and are based at the University of Cape Town or at the Groote Schuur Hospital. Younger scientists who become involved will be adequately trained and supervised by a senior staff member.

Who is paying for this study? Who is paying for this study? This study is carried out on voluntary basis and is not paid for and forms part of a Masters degree.

Can we trust that there is no conflict of interest? In other words, can we be sure that this study is for the benefit of breast cancer patients and not to promote a hidden agenda of a sponsor or a researcher? There are NO conflicts of interest. The findings of this study are for the benefit of breast cancer survivors and will add to our knowledge of the components of axillary web syndrome and how to manage it.

What if something goes wrong during or after the study? The University of Cape Town (UCT) promises that in the event of you suffering in health or well-being caused by you taking part in the study, it will provide immediate medical care.

Procedures and time involved:

Once we receive your reply slip we will contact you about your possible inclusion in the study. If you are able to participate we will then make an appointment for you to attend the Groote Schuur Hospital Radiology Department in Cape Town. This appointment will require about one hour of your time. This will start with a 15 minute information session about the aim of the research project. We will read through the information sheet and answer your questions about the project. If you are interested in taking part in our research project you will be asked to read and sign a consent form. If you agree to take part we will continue as follows:

1. A member of the research team will ask you a few questions regarding your symptoms, areas of tightness and pain and ability to move your arm and shoulder.
2. You will then be asked to undress to your bra and lie down on a table with your arm raised. You will be asked to move your arm into different positions and the range of movement (ROM) will be measured. We will do this for both arms.

3. Then we will take measurements of the cord with a tape measure and photograph it. Your face will not be photographed only your arm and armpit will be in the photographs.
4. A team member will then take ultrasound scans of your arm and armpit with some gel and ask you to hold your arm in specific positions but within your ability and level of pain. The gel can be washed off afterwards. We will also do this for both arms.
5. Lastly, you will fill in a short questionnaire about your current level of pain and functional ability of the arm and shoulder. You may not be experiencing any difficulty, but we will still use your data to compare to those who are having difficulty.
6. After this an appointment with the physiotherapist will be made for you to receive treatment. Subsequent sessions will be made with her.
7. At the end of your last treatment the research team will go through one final measurement cycle with you. In total there are thus two measurement times.

Will I get to see the results? This is a pilot study which may give us more information on the development of the disorder and hints of where to look next. We will not be sending out any results to participants but if you would like to see a summary of the study you may ask us.

Who can take part: To take part in this study you must be a female and older than 18 years of age. You must have been treated for breast cancer, have clear evidence of cording and speak English or Afrikaans. For participating in the MRI procedure, you cannot have a pacemaker or have had a shoulder replacement.

Who will know that I am taking part in this project: Your identity will be kept secret and your personal details will be safely stored in the office of the principal investigator, at the Department of Human Biology, University of Cape Town. The data will be coded with a reference number so that your name and other details cannot be matched with the other data and will not be used in any reports or publications written about this study.
The only person who will know that you are taking part are your health professionals working with the research team.

Will I get paid for taking part: You will not be paid to take part in the study. You will, however, be reimbursed for travelling to the venue where research data is collected.

Are there any risks involved in taking part in the study: The MRI exam may be uncomfortable and unsettling because of the tunnel you are asked to lie in, the noise the machine makes and that you need to lie still for the duration of the scan. We will, however, work as fast as possible to limit the discomfort and give you earphones during the exam to block the noise as much as possible. You are unlikely to experience pain and discomfort during the physiotherapy treatment as treatment is done within your limits of pain. It is carried out by a professional physiotherapist and is a standard procedure. All research measurements taken will also be done within your level of pain and discomfort.

What are the benefits are for me: The direct benefit from the study is that you will get professional physiotherapy treatment and medical attention for your problems. This study aims to observe changes in your symptoms during physiotherapy and may provide information that will be useful in the future to understand what causes the complications and how to improve treatment.

Do I have to take part? NO. It is entirely up to you if you want to take part in this study. You may decide that you do not want to take part or decide to withdraw from the project at any time. This decision will not affect any current treatment you may be receiving.

What if I have other questions now or later about the study or my rights: If you have questions about the study that are not answered in these Information Sheets please ask the interviewer to answer them. If you have any concerns related to this project in the future you may contact:

- the study investigators at the telephone numbers given on the first page
- Professor Marc Blockman, Chair, UCT Human Research Ethics Committee, Faculty of Health Sciences, may be contacted by research subjects to discuss their rights.
  office tel.: 021-4066492; email address:marc.blockman@uct.ac.za.

Reply Slip

PROJECT TITLE: Axillary Web Syndrome (AWS) after treatment for breast cancer: comparing clinical variables with ultrasound imaging data focussing on anatomical changes before, during and after physiotherapy treatment.

I, ………………………………………………………………………….., would like to take part in this study.

My contact details are:

………

………

We will contact you via these details and confirm your inclusion in the study.

Consent Form

PROJECT TITLE: Axillary Web Syndrome (AWS) after treatment for breast cancer: comparing clinical variables with ultrasound imaging data focussing on anatomical changes before and after physiotherapy treatment.

AGREEMENT TO PARTICIPATE

I, ……………………………………., have read (or have had read to me) the Information Sheet for the study named '**Axillary Web Syndrome (AWS) after treatment for breast cancer:** comparing clinical variables with ultrasound imaging data focussing on anatomical changes before and after physiotherapy treatment'.

My role in the study is as a research volunteer to help the investigators collect information about the anatomical structures involved in the development of arm and shoulder complications after treatment for breast cancer. I understand that the purpose of this study is to observe symptom changes during physiotherapy treatment and the information may or may not be useful in designing better ways to treat these complications in the future. My questions have been answered to my satisfaction in a language that I understand. By signing this consent form I do not waive any of my rights.

I, ……………………………………., **AGREE** to take part in the study '**Axillary Web Syndrome (AWS) after treatment for breast cancer:** comparing clinical variables with ultrasound imaging data focussing on anatomical changes before and after physiotherapy treatment'**.**

(initial boxes where appropriate)

I authorise my doctor and other health care professionals to provide relevant clinical details to the research team of this study. ☐

I authorise photographs of my armpit and arm to be taken and used in publications. ☐

Research Volunteer:

Signature: ……………………………………..

Date: …………………………………….. Volunteer: Please sign both copies of this page

Name: ……………………………………..
Please Print

Interviewer Obtaining Consent:

Signature: ……………………………………..

Date: …………………………………….. Interviewer: Please sign both copies of this. page and hand one copy back to the research volunteer

Name: ……………………………………..
Please Print

Appendix C: Data Collection Sheet A(i): Measurement

Date: 04-06-2013 Version: 02

I

Participant #:
Date:

Dominant hand:	Left		Right
Symptoms:	Cording	↓ROM	Pain

Pre-treatment

Cord characteristics:

Cord 1 side:	Left		Right		
Localisation (°):					
Width (cm):					
Length (cm):					

# of cords:					
Cord 2:					
Localisation (°):					
Width (cm):					
Length (cm):					

ROM measurements:	Left		Right	
Scaption (°):				
Horizontal adduction (°):				
Flexion (°):				
Extension (°):				
Internal rotation (°):				
External rotation (°):				

SPADI score:	
Photograph #:	
Ultrasound Scan #:	

II

Treatment #:
Date:

Symptoms:	Cording	↓ROM	Pain

Post-treatment

Cord characteristics:

Cord 1 side:	Left		Right		
Localisation (°):					
Width (cm):					
Length (cm):					

# of cords:					
Cord 2:					
Localisation (°):					
Width (cm):					
Length (cm):					

ROM measurements:	Left		Right	
Scaption (°):				
Horizontal adduction (°):				
Flexion (°):				
Extension (°):				
Internal rotation (°):				
External rotation (°):				

SPADI score:	
Photograph #:	
Ultrasound Scan #:	

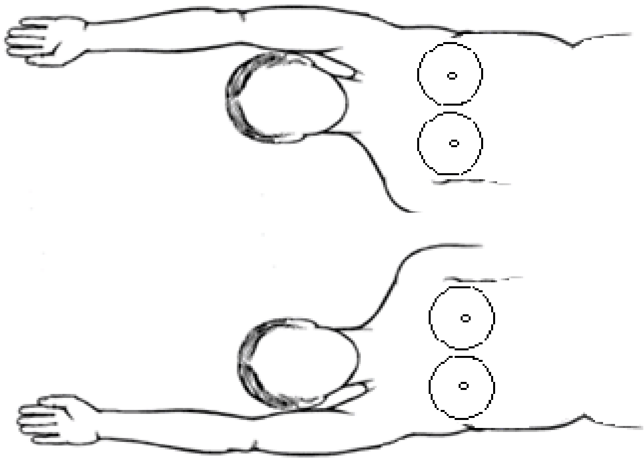
Appendix D: Data Collection Sheet A(ii): Cord Location

Date: 04-06-2013 Version: 02

I

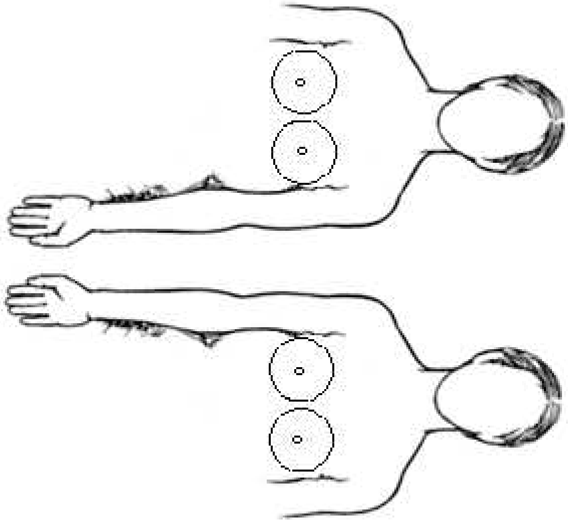
Participant #:		**Operated side:**	Left	Right
Date:		**Scar location:**		

Pre-treatment



L

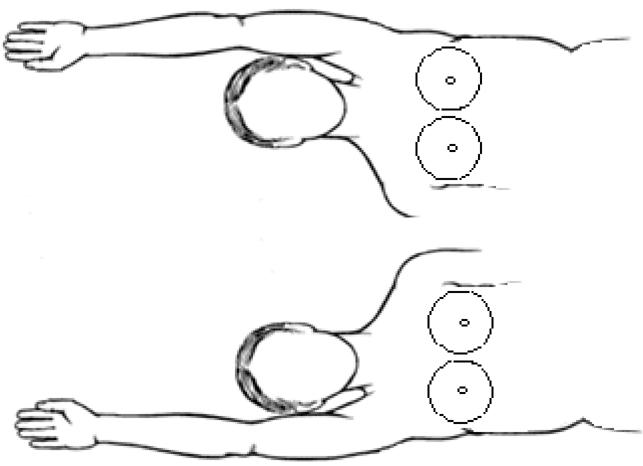
R



II

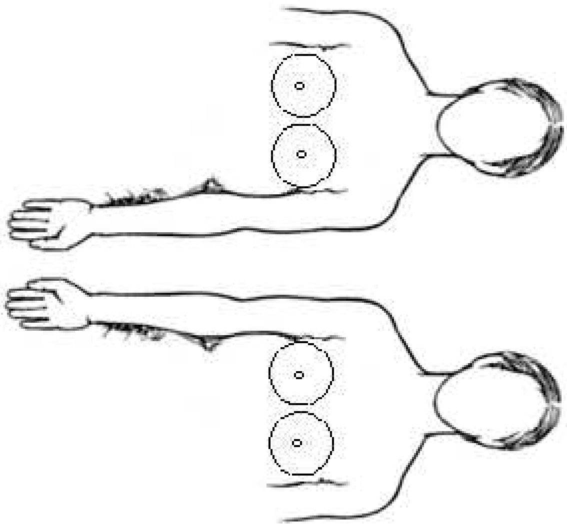
Treatment #:	
Date:	

Post -treatment



L

R



Appendix E: Data Collection Sheet B: Clinical and Demographic

Date: 04-06-2013 Version: 01

Demographics

Participant #:		Weight (kg):	
GSH file #:		Height (m):	
RT file #:		BMI (kg/m^2):	
Physiotherapy file #:		Birth date:	

Clinical

	Cancer							
Type:								
Stage:	I		II		III		IV	
Tumour type:	Invasive ductal	Tubulolobular	Mucinous	Comedo	Lobular	DCIS	Tubular	NOS
Tumour size (mm):								

	Tumour			
Tumour:	T1	T2	T3	T4
Lymph nodes:	N1	N2	N3	
Metastasis:	M0	M1		
If M1, to where:				
# Resected nodes:				
Type of nodes:				

Receptor status:	**ER:**	Positive	Negative	**PR:**	Positive	Negative

	Surgery
Surgery type:	
Tissues removed:	
Procedure date:	

	Radiotherapy	**Chemotherapy**	**Hormonal therapy**
Dose intensity (Gy):			
# Fractions:			
Dose frequency:			
Total doses:			
Field of radiation:			
Start date:			
End date:			

	Physiotherapy
Start date symptoms:	
Time since surgery:	
Time 1st treatment since surgery:	
Total treatments:	
Time to resolution:	
Symptom recurrence:	

Appendix F: Data Collection Sheet C: Physiotherapy Details

Date: 04-06-2013 Version: 01

1

Participant #:

Date:

Treatment session 1

Treatment specifications:

Homework protocol:

Improvements/setbacks:

Functional limitations:

Compensatory actions:

Areas of pain and/or tightness:

2

Treatment #:

Date:

Treatment session 2

Treatment specifications:

Homework protocol:

Improvements/setbacks:

Functional limitations:

Compensatory actions:

Areas of pain and/or tightness:

3

Treatment #:

Date:

Treatment session 3

Treatment specifications:

Homework protocol:

Improvements/setbacks:

Functional limitations:

Compensatory actions:

Areas of pain and/or tightness:

Appendix G: Physiotherapist Notes

Physiotherapy details

Participant no.	Treatment no.	Date	Complained of	Objective assessment	Treatment
FS/2013/01	1	23/10/2013	having 3rd chemo on 25/10/2013, does light chores, pulls++ on L chest wall with arm mvts	bilat horizontal mastectomy incisions, more puckering on L Elevation: L 150^0 R 170^0	scar massage to release adherence areas L & R MFR across chest wall with arm in elevation L & R L – fascial releasing into axilla and upper arm on L with arm supported in elevation Taught mobilising and stretch exercises to do at home
	2	6/11/2013	felt good after Rx till chemo then tight again	scarring tight, quite adherent to chest wall ROM L - 160^0	focussed on releasing scar on L as well as tight fascia Exercises Breathing and relaxation
	3	8/11/2013	easier since Rx		MFR across chest wall in supine (pecs) and R side ly – serratus ant and post Passive scapular mobilisation and active retraction in side ly Side ly – progress to full elbow ext – neural stretch Exercises and breathing
	4	13/11/2013	feels tightness in L arm and into chest after doing housework	minimal cording visible but restriction felt and seen with elevation + elbow ext	strong stretches + fascial release of chest wall, into axilla and upper arm → much freer still slight pull in upper arm with overpressure Exercises: progressed to wt bearing in 4 Pt kneeling, alt arm and leg stretch, cat stretch, shell stretch and table top stretch in standing
	5	11/12/2013	feeling better, doing well with stretches, arm asymptomatic	very little cording visible on full elevation with full elbow and wrist Ext. pull felt in upper inner arm	checked on exs

FS/2013/02	1	29/10/2013	pain in arm, sometimes down to wrist when has used arm. Is a nurse aid, unable to work at the moment but hopes to return to nursing once treatment over	All sh mvts restricted Elevation through Fl - 150^0, HBH most limited functional mvt due to limited ext rot - 45^0 Palpation –scar very adherent on chest wall – restriction of skin and superficial fascia Cording ++ visible - tight band extends from chest wall above scar across axilla and into antero-medial aspect upper arm → pulls ++ down towards elbow with elbow E with arm in elevation Scap mvts very restricted	Scar tissue massage along length of scar Fascial release over chest wall – very adherent to ?? deep fascia MFR to pec maj and minor, coracobrachialis, short head of biceps Fascial release into axilla Exercises to encourage scapular movements
	2,3,4	6/11/2013, 13/11/2013, 20/11/2013			Scar massage MFR – ant and posterior – serratus ant, infraspinatus, latissimus, rhomboids, lev scap and trapezius Trigger point release TPs in infraspinatus and serratus ant. Neural mobilisation of median nerve Also MFR down upper arm and forearm Fascial release across chest and into axilla, upper armExercises and stretches ++
	5	27/11/2013	feeling better – been more active Pulls medial aspect forearm with full elbow extension as when bending down to pick something up	Elev - 165^0 - tight across elbow and into med aspect forearm ↓ ROM elbow on full elev -10^0 elbow ext	MFR ++ across chest wall over pec minor and long head of biceps Side ly – scap mobs, activation of lower traps, rhomboids. Release of post axillary structures and triceps Exercises – progressed to 4 pt kn, alt arm and leg stretch, shell stretch
	6	20/1/2014	Finished radiotherapy – caused tightness ++ across chest wall	ROM - 160^0	gentle massage over chest due to skin still being ‘sunburnt’ Side ly – scap mobs and MFR of scap/tx muscles Exercises Breathing and relaxation

	7	29/1/2014	feeling better again – being more active and arm less 'tight'	ROM elev - 165^0 restriction due to adherence on chest wall → tight bands into axilla and upper arm.	vigorous releasing and stretching – most pain experienced in forearm (neural)
FS/2013/04	1	6/11/2013	uses arm but is cautious 'does not know what she can/can't do' does not want to cause harm	ROM: Elevation L – 160 R – 150 but unable to extend elbow →- 15^0 E Obs – very tight, ugly scar on R chest wall with puckering and adherence to chest wall Has not touched or washed area since radiotherapy as was told not to. Thoracic kyphosis – restricts sh mvts	Scar massage ++++ → removal of dead and discoloured layers of skin Gentle fascial release over chest wall Stretching exs
	2	13/11/2013	very happy with the improved appearance – has made her feel better.	no change in ROM – very 'stuck'	Scapular mobilisations – very tight and stuck
	3	20/11/2013	feeling easier, using arm more freely	ROM – no change Skin better and looser	scar massage MFR – pecs, coracobr Fascial release over chest wall down onto attachments of diaphragm, extending into axilla and upper arm – pulls++ at limit of range Stretching exs
	4	4/12/2013	doing well, feeling good	no change in ROM Scap mvts very restricted	Release of scap m's in side ly and activation of stabilisers
	5	11/12/2013		No change	MRF ++ also Serratus ant, upper traps, infrasp Fascial release – pec minor Release of cord into axilla and upper arm Stretches ++
	6	5/02/2014	has been fine, happy with what has been achieved with physio	scapula mvts freer - has maintained the improved range and function cord still visible in axilla at full range	fascial release a/a Scapular stabilisation Stretches

FS/2013/07	1	27/11/2014	R arm does not feel right – feels a pull down the upper arm and across elbow Also feels a pain 'inside' arm and into thumb	extremely anxious and guarded about using R arm beyond 90^0 elev ROM – Elev - free active 100, active assisted – 150Tightness ++ in axilla and extends to med aspect upper arm – taught band Scar fairly tight at meduial end and puckered lat end ↑ thoracic kyphosis restricts sh range	scar massage Fascial release front of chest wall MFR – pecs and into upper arm Exercises
	2	5/12/2013	feels much improved, arm feels normal, no longer anxious to use it.	Active ROM – 150	more vigorous scar massage and fascial release on chest wall above scar and towards axilla Scapular mobilisation in side lying + MFR serratus ant Exercises Scar massage
	3	15/01/2014	feeling good, has managed well Had an episode of swelling R upper arm + pain med aspect towards elbow 1 week ago – spontaneous resolution – has occurred before ? related to bouts of overuse??	maintained range well ROM elev 160 = Full range due to tx kyphosis which limits full elev Abd 90 HBB L = R HBH L = R (ie normal for the patient) but ?? L sh dysfunction)	Fascial release around scar to under lower ribs/diaphragm MFR –across chest to axilla + upper arm Stretch with arm in elevation → good release of cord in axilla → ↑ range → slight pull in upper arm on full elevation + wrist ext Stretching exs
	4	22/01/2014	inner upper arm & forearm feel tight	pain on elbow ext, sh elevation - appears neural (has been a bit stressed)	extensive fascial release – chest wall, axilla and upper arm in supine with arm in elev. → Neural mobs with sh in elev – some relief of upper arm Sx → facial release down arm into flexor retinaculum forearm → improvement Side ly – Cx Sp mobs C2 - pain Tx mobs – T8 very tight and painful Scap mobs and 'setting' with activation of stabilisers Stretching exs→ symptoms relieved

	5	29/01/2014	pain went away next day – no problems since Arm asymptomatic	ROM elev 160 but mvt feels much freer and no pain/tightness Cord still visible in axilla on elev	specific fascial relwease over incision & into axilla where cord is still visible with arm in elev-good response – tissues less taught & no pull in upper arm.MFR serr ant & rhomboids Scap mobilisation & scap setting Exs – stretches + wt bearing thru shoulders to stimulate stabilisers
FS/2013/08	1	12/30/2014	bilateral shoulder pain R > L x 1 year R knee osteoarthritis – waiting for a knee replacement Also 'slipped disc' – low back pain	horizontal mastectomy incision, adherent to chest wall medially Skin very discoloured from radiotherapy, has not been washing the area so a lot of old dry skin and scabs along incision Active elevation in standing: L 150^0 R 120^0 Active Abduction in stand L 80 R 70 Altered scapulao – thoracic rhythm noted with mvts in standing, poor control	general massage with oil to clean up area of old skin etc Deep scar massage to release adherence medially as well as thickened area between scar and axilla where there is extensive adherence MFR across chest wall with arm in elevation R Taught mobilising and stretch exercises to do at home
	2	9/04/2014	recovering from gastic flu, has not done exs	no change except in appearance of the area due to clearing of old skin etc	focussed on releasing very tight areas along scar as well as tight areas above R – fascial releasing into axilla and upper arm on R with arm supported in elevation Taught shoulder mobilising exercises as well as stretches to maintain
	3	23/04/2014	feeling easier since Rx	slight improvement in elev R – 130, functional activities like dressing a bit easier.	scar tissue release – area above and below scar are very thickened and adherent ++ MFR across chest wall in supine (pecs) and L side ly – serratus ant and post Passive scapular mobilisation and active retraction in side ly MFR into axilla and upper arm + stretches ++ Exercises
	4	14/05/2014	has had a lot of fibromyalgia – not moving around much so has stiffened up	pre treatment elevation in lying = 150 Post treatment = 160 (has difficulty maintaining this improvement week to week)	Rx a/a – ++ MFR and stretching with arm in elevation - not much response by tissues to fascial releasing. Exercises: as usual,

	5,6	29/05/2014, 11/06/2014	finds cold weather affects her arthritis – stiff joints	Elev in standing – 130	Rx a/a – extensive strong fascial releasing as well as passive stretching with arm in elevation as well as side lying with scapular protraction & retraction. ---- Pulls down inner upper arm – range also restricted by shoulder pathology in supine ly Checked on exs and emphasised home exercises.

Note: It has been difficult achieving significant objective changes with FS/2013/08 due to several factors:

- Length of time since surgery so tissues not responsive to change
- General OA and fibromyalgia
- Increased BMI
- Lack of motivation to do home exs or massage

Subjectively, I felt there were subtle changes in the structures crossing the axilla and marginal reduction in the thickening of skin folds above the incision.

FS/2013/11	1	4/07/2014	some difficulty reaching top shelf, drying hair, otherwise manages all ADL Does protect her L side	Elev R 180 L 160 Ab 90 90 Lat Rot 50 40 HBB 115 100 (hand behind back) cord visible in lower aspect axilla on full elevation in lying (unusual as commonly higher up towards humerus) Palpable superficial lump in mid axilla – soft, not tender …?? Low BMI so no puckering or thickening of excess tissue along scar area. Slightly tight and adherent to chest wall	scar tissue massage MFR - pec major,(supine) and lat dorsi and scapular muscles in side ly Fascial release of cord and 'lump' Stretching exs taught
	2	14/07/2014	'feels easier', using arm more freely	MFR +++ lat border of pec major, pec minor(tender) lat dorsi insertion posterior axillary wall fascial release of cord in axilla and attachements to adipose tissue Full stretch into elevationwith fascial and neural releasing Pec and lat dorsi stretches	elevation in lying – 170 – slight tightness at full range

		3,4,5,6	23/07/2014, 4/08/2014, 11/08/2014, 18/08/2014	See previous	achieved full range of shoulder elevation, reduced pull into axilla with full range movements. Cording reduced visibly as well in axilla and the fat pad softened and became smaller and flatter. Good compliance with home exercises as well as her confidence in herself contributed to what I perceive to be a successful treatment intervention.	See previous
FS/2013/03	Did not want to continue with physio after measurement cycle due to socioeconomic and personal problems					
FS/2013/05	Cord resolution but socioeconomic and personal problems prevented her from continuing					
FS/2013/06	Too ill to continue with physiotherapy					
FS/2013/09	Cord resolution but socioeconomic and personal problems prevented her from continuing					
FS/2013/10	Did not respond to calls for physiotherapy					

Appendix H: Table US Analysis

This table demonstrates the indicators used in ultrasound analysis of each patient.

Affected Side versus Unaffected Side - Before Physiotherapy													
	Patient number												
Variable	**1(L)**	**1(R)**	**2**	**3**	**4**	**5(L)**	**5(R)**	**6**	**7**	**8**	**9**	**10**	**11**
Thickened/ hyperechoic SF	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Thickened/ hyperechoic DF	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Coarse homogeneity AT	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Muscle artefact	✓	✓		✓				✓		✓	✓	✓	✓
Increased connections dermo-hypodermic junction	✓												
Increased connections SF-DF-muscle	✓												
Disorganisation in AT	✓					✓	✓						
Decreased number of layers	✓		✓	✓	✓	✓	✓						✓
Patch of (course) homogeneity	✓	✓				✓	✓					✓	✓
Fibrous scar						✓	✓						
Arch during tensioning				✓									
Honeycomb organisation SF													
Increased heterogeneity													

Appendix I: Most at Risk for Fibrosis Table

A summary of the different treatments (radiotherapy, chemotherapy and hormonal therapy) and their contributing risk at developing fibrosis. The # = the rank attributed according to the number in the previous column with 1 attributed to the highest – 11 to the lowest. The accumulative risk is the term describing the final position of the risk on all the measures combined compared to the other participants and is dependent on the total rank: the lower the total rank, the more potential risk the patient has at developing fibrosis, the higher the accumulative risk. Although the author acknowledges the necessity of knowing the quantities of each drug taken, the treatment regimens were of similar dose and the ranking are more a relative indicator rather than absolute.

Most at risk for fibrosis ranking

Participant no.	Radiotherapy dose (Gy)	#	Chemotherapy types of treatments	Chemotherapy no. of treatments	#	Hormonal therapy types of treatments	#	Total rank	Accumulative risk	Comparison improvem table
FS/2013/01		5	Gemcitabine/ CEF	2/4	5		4	14	Best	best/ best
FS/2013/02	41,6 + 38,4*	1	CEF/ Paclitaxel	3/4	2		4	7	Worst	Worst/ 5
FS/2013/03	42,7	3	CAF/ Paclitaxel	6/6	1		4	8	Fifth	
FS/2013/04	42,72	4	CEF	6	7	Tamoxifen/ Arimidex	3	14	Best	best /4
FS/2013/05		6	CAF/CMF	6/6	3	Tamoxifen/ Arimidex	3	12	Third	
FS/2013/06	47/ 20	2	CAF/ Vinorelbine	6/6	5	Tamoxifen/ Exemestane/ Arimidex/ Provera	1	8	Fifth	
FS/2013/07	47	3	CAF	6	6	Tamoxifen	2	11	Fourth	2 / 2
FS/2013/08		6	CEF/ Taxotere	3/3	4	Tamoxifen/ Arimidex	3	13	Second	4 /3
FS/2013/09	47	3	CAF	6	6	Tamoxifen	2	11	Fourth	
FS/2013/10	42,72	4	CAF	6	6	Tamoxifen/ Arimidex	3	13	Second	
FS/2013/11	42,72	4	CAF	6	6	Tamoxifen	2	12	Third	3 /worst

*patient received two different doses of radiotherapy to two different areas during the physiotherapy treatment and had to stop the treatment for some time to recover.

Although treatment regimens are dependent on the cancer type and severity, they have also been shown to pose a potential risk of developing fibrosis due to their destructive ability. The table is therefore not an absolute indicator of fibrosis development but ranks the patients according to who might be more at risk due to previous findings in the literature on the development of fibrous tissue. For example, when the radiation dose is higher and in the case of specific chemo- and hormonal therapy regimens. This might also give an indicator on the propensity of recovery after physiotherapy as less fibrotic tissue formed will require less effort to resolve and should be compared to the improvement table. This seems to mirror some of the information especially in the extreme cases – indicating some relationship trend between these values. Other factors such as the lifestyles of these individuals that may worsen their condition could not be evaluated and thus this table is not conclusive and only a guideline.

Appendix J: Most Improved Ranking Table

SPADI Pain and Disability (Dis.) scores on the affected arm. The # = the rank attributed according to the number in the previous column with 1 attributed to the highest – 7 to the lowest. The accumulative improvement is the term describing the final position of how the participant improved on all the measures combined compared to the other participants dependent on the total rank: the higher the total rank, the least the participant improved, the lower the accumulative improvement.

Improvement ranking after physiotherapy																	
Participant no.	Cord length (%)	#	Abduction (%)	#	Extension (%)	#	Forward flexion (%)	#	External rotation (%)	#	Internal rotation (%)	#	SPADI (Pain) (%)	#	SPADI (Dis.) (%)	#	Total rank	Accumulative improvement
FS/2013/01* (left)	100,00	1	78,13	3	133,33	2	46,00	2	24,21	5	26,32	4	84,62	4	92,31	1	22	Second
FS/2013/01* (right)	100,00	1	130,14	1	150,00	1	29,60	3	30,95	4	36,94	3	60,00	6	71,43	2	21	Most
FS/2013/02	34,63	2	47,83	6	8,16	4	-0,88	7	-33,33	7	-8,77	6	87,88	3	69,01	4	39	Sixth
FS/2013/04	100,00	1	48,91	5	6,78	5	77,81	4	40,35	3	-5,88	5	66,67	5	0,00	7	35	Fifth
FS/2013/07	100,00	1	97,01	2	106,25	3	18,00	1	44,32	2	53,27	2	42,86	7	38,46	6	24	Third
FS/2013/08	-15,96	4	38,27	4	-14,06	7	6,31	6	109,80	1	500,00	1	87,88	2	71,11	3	28	Fourth
FS/2013/11	30,35	3	10,07	7	-11,29	6	16,67	5	-24,24	6	-11,76	7	100,00	1	50,00	5	40	Least

*Patient FS/2013/01 had both left and right arms affected

Number of physiotherapy treatment was approximately equal for all patients and were at the discretion of the physiotherapist on the team to decide whether more treatments would be beneficial to the patients. This is a relative ranking as the ranks do not take into account differences between the patients.